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AND ECONOMIC OUTCOMES BETWEEN THE ARMY, AIR FORCE, AND NAVY

By

David M. Bennett

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As members of the Final Examination Committee, we certify that we have read the dissertation prepared by David M. Bennett entitled EFFECTIVENESS OF CLINICAL PRACTICE GUIDELINES FOR TREATING ASTHMA IN THE DEPARTMENT OF DEFENSE: A COMPARISON OF CLINICAL AND ECONOMIC OUTCOMES BETWEEN THE ARMY, AIR FORCE, AND NAVY.

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I hereby certify that I have read this dissertation prepared under my direction and recommend that it be accepted as fulfilling the dissertation requirement.

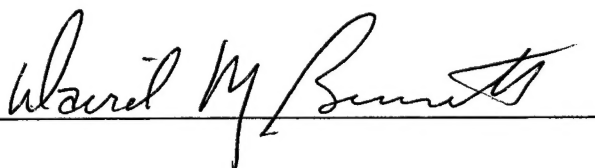
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SIGNED: _____

A handwritten signature in cursive script, appearing to read "David M. Bennett", is written over a horizontal line.

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Disclaimer

The views expressed in this dissertation are those of the author and do not reflect the official policy or position of the United States Air Force, Department of Defense, or the U.S. Government

DEDICATION

This dissertation is dedicated to my family — [REDACTED] Thank you for your love, support, encouragement, and patience. Sending an old man back to school is not easy, but you have persevered with me to the end. Because of you - my wife and my sons - I can truly say that I am a lucky and blessed man.

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ABSTRACT

The purpose of this research was to evaluate the strategy of the military health service (MHS) to improve asthma outcomes through the use of clinical practice guidelines (CPGs). Outcomes were evaluated at the patient level and included inpatient/outpatient visits, prescriptions dispensed, number of exacerbations, number of beddays and direct cost of therapy. In addition, provider compliance to CPG recommendations was evaluated by measuring the proportion of subjects dispensed long-acting controller medications. A nonrandomized control-group before-after design with retrospective matched-pair DoD data was used for this research. The intervention used in this research was the formal asthma CPG-use process implemented by the Army in September of 2000.

Compared to baseline measures, all outcomes improved significantly ($p < 0.05$) in the after period for both the subjects exposed, and not exposed, to the CPG-use process. Other than the improvement noted in the number of asthma exacerbations, which was greater in the exposed group than the non-exposed group ($p < 0.001$), there was no other difference between groups in the amount that outcomes improved.

When adjusted for covariates (gender, comorbidity, age, beneficiary status, facility size, TRICARE region, multiple facilities, and treatment received at a lead agent facility), the CPG-use process was associated with a decrease in the direct cost of asthma therapy

(-\$55.65, $p = 0.021$). There was no association between the Army CPG-use process and total number of encounters, prescriptions, or beddays. Health care visits (0.12, $p < 0.001$) and exacerbations ($OR = 1.22$, $p < 0.001$) were significantly higher for those exposed to the CPG-use process as compared to those not exposed.

The proportion of subjects prescribed long-term controller medications increased significantly for subjects exposed to the CPG-use process (0.30 to 0.66, $p < 0.001$), and for those not exposed to the CPG-use process (0.30 to 0.66, $p < 0.001$).

Although the findings of this research suggested that a formal CPG-use process to standardize asthma therapy was associated with decreased costs, this was not supported by results regarding the clinical outcomes. To further evaluate the effect of asthma CPGs on economic and clinical outcomes, additional research is needed.

Chapter 1

Introduction

1.1 Background

Despite advances in medical knowledge and treatment strategies over the past two decades, both the prevalence and morbidity of asthma have continued to increase in the United States and around the world.(1) It is not clear whether these changes reflect a true increase in the prevalence of asthma or a change in the diagnosis - partly due to changes in the International Classification of Diseases (ICD) schema.(2) Nevertheless, asthma is estimated to affect about 15 million Americans, one-third of them children.(3) It is the most common chronic childhood illness and the leading cause of pediatric hospitalizations.(4)

It was reported that asthma is associated with more than 100 million days of restricted activity each year.(4) Asthma accounts for more absenteeism by school children than any other chronic condition, about 10 million school days annually. Lost productivity, stemming from worker absenteeism has been estimated to have cost the United States over \$1 billion annually (1990 dollars).(4) Total direct and indirect costs associated with asthma were estimated at \$6.2 billion in 1990, with emergency room visits, hospitalizations, and premature mortality accounting for 43% of the total expenditures.(4) By 1998, the estimated costs associated with asthma in the United States had increased to over \$12 billion.(5)

Asthma impacts the Department of Defense (DoD) in several ways. First, it is a readiness issue for active duty and reserve military troops. This was evident in the early 1990's with the inability to deploy over 500 U.S. Army soldiers with an asthma diagnosis to Operation Desert Storm, and the evacuation of more than 200 others who experienced asthma related problems once they that had been deployed.(6)

Asthma has long been considered a reason for disqualification from military service. Of the 30 percent of applicants that were disqualified for military service in World War II, two percent of them were for asthma.(6) Before 1995, the U.S. Department of Defense (DoD) allowed individuals with a history of asthma, but whose symptoms had ceased by age 12, to enter the military. In August of 1995, the entrance criteria became more stringent, making a diagnosis of asthma at any age grounds for disqualification for military duty. This was not an iron clad directive, however, as some individuals with a history of asthma did obtain a medical waiver. Although the factors for obtaining a waiver varied between services, such things as absence of asthma symptoms since the age of 12 years, successful participation in high school athletics without asthma symptoms, and evidence of high motivation, were usually considered.(6)

The unpredictable nature of the military lifestyle makes asthma particularly problematic in the DoD. Extremes of temperature, humidity, stress, exercise, smoke, and fumes are unavoidable in many military jobs and are frequently triggers for asthma exacerbations.(7) Additionally, depending upon a service member's duty assignment or

deployment status, access to care by a medical officer may not always be readily available. From the perspective of the military service, any disease that can cause disqualification of highly trained individuals from duty represents an opportunity cost. Some authors have suggested that, regardless of current examination findings, any history of childhood asthma should be grounds for disqualification for certain specialties like aviators, due to the great expense and danger associated with these training programs.(8) Published estimates of asthma prevalence in the US military range from a low of less than one percent in military members assigned to submarine duty, to a high of six percent in a study reporting exercise-induced airflow obstruction in US Air Force members.(9, 10)

Apart from the recruitment, eligibility, and treatment issues of asthma in the active duty force; the military health service (MHS) also has health care responsibilities for those in the dependent and retiree sectors of the DoD population. In fact, according to one report, dependents and retirees make up close to 80 percent of the eligible population served by the MHS.(11) The health care issues of this population range widely, from the pre- and perinatal needs of young mothers and infants to the needs of an aging DoD population.(12) Included in all these issues are the concerns of chronic conditions such as asthma.

1.2 Statement of Problem

TRICARE is the DoD's worldwide managed health care program mandated by Congress through various legislative actions. Its goals are to improve access to care, assure high-quality health care, provide more choices, and contain costs.(13) These are daunting challenges, especially considering the broad range of geographical and operating environments over which the MHS is required to provide care. To achieve these goals, the TRICARE program has restructured the MHS into health service regions (HSRs), each administered by a lead agent who is affiliated with a military teaching hospital. The lead agent, together with the governing board made up of the commanders of the military treatment facilities (MTFs) within a particular HSR, is responsible for implementing an integrated plan for the delivery of health care to the beneficiaries.(12) Achieving efficient and cost-effective care for those treated within and between HSRs has been a primary objective of the MHS. Standardization of care, through outcomes management and the implementation of clinical practice guidelines (CPGs) for key disease states, has been one strategy used by the MHS to meet these objectives.

Beginning in 1998, the Army Medical Department initiated a comprehensive effort to implement CPGs across all Army MTFs. Although mandatory for Army MTFs, participation by Navy and Air Force MTFs was voluntary. One of the disease states considered appropriate for CPG development and implementation was asthma. The DoD asthma guidelines, developed jointly with the Veteran's Administration, were adapted from those developed by the National Heart, Lung, and Blood Institute (NHLBI) and

implemented in September of 2000 at all Army MTF's.(3) The primary demonstration sites of the asthma guideline implementation project were: Eisenhower Army Medical Center at Ft Gordon, Georgia; Martin Army Community Hospital at Ft Benning, Georgia; Blanchfield Army Community Hospital at Ft Campbell, Kentucky; and Moncreif Army Community Hospital at Ft. Stewart, South Carolina.(14)

Consistent with reports in the literature that state that a disproportionate amount of effort is placed on the development of guidelines, compared to their implementation and evaluation, little has been published evaluating how asthma CPGs meet the needs and expectations of the MHS in terms of improving clinical and economic outcomes.(15) Since the military health services operate on a fixed budget, it is important that the outcomes of health care initiatives, such as the asthma CPG project, be quantified, so that future health care resources can be allocated by MHS decision makers in an efficient manner.

1.3 Significance of Problem

Clearly, as with other sectors of our society, the cost of delivering health care to the beneficiaries of the DoD Military Health System has become a very expensive proposition. It was reported in 1996 that nearly 25 percent of the entire DoD budget was allocated to financing health care for its beneficiaries.(16) Another report, for the same year, placed this amount at over \$15 billion(11). As further evidence of the high costs associated with treating asthma, the DoD Pharmacoeconomic Center (PEC) reported that

the cost of supplying asthma medications to DoD beneficiaries in 1996 exceeded \$19 million.(17)

In addition to, and linked with the monetary expense of providing health care, are the issues of quality of care, risk management, and improved clinical outcomes. It is estimated that over 21 percent of all asthma hospitalizations could be avoided in the 15 to 44 year age category, and 15 percent avoided in the 45 to 64 year age category, if treated properly.(18) Further, the rate of 'activity limited days' due to asthma appears to be related to quality of care.(19) The CPG Program, developed by the MHS to address these issues, has the potential to significantly reduce MHS costs by employing standardized and cost-effective therapy.

1.4 Purpose of Study

The purpose of this study was:

1. To determine if standardizing care through the use of clinical practice guideline had an impact on the clinical and economic outcomes of those treated for asthma within the military health system of the United States.
2. To determine whether the extensive asthma clinical practice guideline implementation and monitoring program used by the Army Medical Department resulted in better economic and clinical outcomes than for the Air Force or Navy.

1.5. Research Questions:

This research project was designed to answer the following research questions:

1. What is the association in the DoD between guideline use and the direct costs of treating asthma?
2. What is the association in the DoD between guideline use and having an asthma related health care encounter as defined as an outpatient visit, an inpatient visit, or an asthma related prescription.
3. What is the association in the DoD between guideline use and having an asthma related health care visit as defined by inpatient and outpatient visits only.
4. What is the association in the DoD between guideline use and the risk of experiencing an asthma exacerbation?
5. What is the association in the DoD between guideline use and the number of prescriptions dispensed for the treatment of asthma?
6. What is the association in the DoD between guideline use and the length of hospital stay for a patient admitted with a primary diagnosis of asthma?
7. What is the association between guideline use and the use of long-term controller medications in asthma therapy?

1.6 Definitions

For this study, the following definitions were used:

Asthma Exacerbations: Acute or sub acute episodes of progressively worsening symptoms such as shortness of breath, cough, wheezing, or chest tightness that often lead to respiratory distress. The severity of these episodes and their management strategies depend on the extent of deterioration in lung function and the response to initial therapy with β_2 -agonists. In this study, the term 'exacerbations' refers only to those episodes which require patients to be treated in an acute care facility such as an emergency room or hospital.

Clinical Practice Guideline: Systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.

Standard Ambulatory Data Record: An electronic administrative database used by the Military Health Service to uniformly collect ambulatory care data across the medical services of the Army, Navy, and Air Force through the use of Physician's Current Procedural Terminology (CPT-4) codes.

Standard Inpatient Data Record: An electronic administrative database used by the Military Health Service to uniformly collect ambulatory hospitalization data across the medical services of the Army, Navy, and Air Force through the use of Standard ICD-9 codes.

Uniformed Services Prescription Database (USPD): A data warehouse of medications dispensed to U.S. Military service members, dependents, and retirees from Military Treatment Facilities.

TRICARE: The managed care system utilized by the Department of Defense Military Health System to deliver health care to over eight million eligible beneficiaries. Divided into eleven regions in the continental United States and three overseas regions, TRICARE is administered mainly through a network of military hospitals (80) and clinics (513) with augmentation provided through civilian facilities and providers.

Physician's Current Procedural Terminology Codes (CPT-4): CPT Codes describe medical or psychiatric procedures performed by physicians and other health providers. The codes were developed by the American Medical Association (AMA) to assist in the assignment of reimbursement amounts to physician insurance carriers.

International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 CM)
A system designed for the classification of morbidity and mortality information for statistical purposes, and for the indexing of medical records by disease and operations, and for data storage and retrieval.(20)

1.7 List of Acronyms:

The following is a list of abbreviations or acronyms that are used in this dissertation:

AFSC – Air Force specialty code

AHCPR – Agency for Health Care Policy and Research

AMA – American Medical Association

AMCC – American Medical Center Consortium

AMEDD – Army Medical Department

ARS-Bridge – All Region Server Bridge

BCBC – Blue Cross and Blue Shield

CDC – Centers for Disease Control

CEPRP – Civilian External Peer Review Program

CHCS – Composite Health Care System

CHAMPUS – Civilian Health and Medical Program of Uniformed Service

CHES – Center for Health Education and Studies

CHPPM – Center for Health Promotion and Preventive Medicine

CMIS – CHAMPUS Medical Information System

CMSS – Council of Medical Specialty Societies

CPG – Clinical practice guideline

CPT-4 Code – Physician's Current Procedural Terminology (Fourth Edition)

CQI – Continuous quality improvement

DATTA – Diagnostic and Therapeutic Technology Assessment Program

DEERS – Defense Enrollment Eligibility Reporting System

DMIS – Defense Medical Information Systems

DoD – Department of Defense

DRG – Diagnostic related group

EBC – Enrollment based capitation

EBG – Evidence-based guideline

EBM – Evidence-based medicine

EI/DS – Executive Information/Decision Support Program

EPR-1 – 1991 NAEPP Expert Panel Report

EPR-2 – 1997 NAEPP Expert Panel Report

FDA – Food and Drug Administration

FEV₁ – Forced expiratory volume in one second

FSS – Federal Supply Schedule

GINA – Global Initiative for Asthma

HCFA – Health Care Financing Administration

HEDIS – Health Plan Employer Data and Information Set

HMO – Health Maintenance Organization

HSR – Health Service Region

ICD-9-CM – International Classification of Diseases 9th revision, Clinical Modification

IHS – Indian Health Service

IOM – Institute of Medicine

IRLS – Iterative Re-weighted Least Squares Regression

JCAHO – Joint Commission on the Accreditation of Healthcare Organizations

MEDCOM – Army Medical Command

MEPERS – Medical Expense Performance Reporting System

MHS – Military Health System

MTF – Medical Treatment Facility

NAEPP – National Asthma Education and Prevention Program

NAEP – National Asthma Education Program

NCQA – National Committee on Quality Assurance

NHLBI – National Heart, Lung, and Blood Institute

NIH – National Institutes of Health

NMOP – National Mail Order Pharmacy

NCQA – National Committee on Quality Assurance

NMES – National Medical Expenditure Survey

OLS – Ordinary Least Squares Regression

PBGH – Pacific Business Group on Health

PDSA Cycle – Plan, Do, Study, Act Cycle

PDTS – Pharmacy Data Transaction Service

PCM – Primary Care Manager

PEC – Pharmacoeconomic Center

PEF – Peak Expiratory Flow

PF – Peak Flow

PPRC – Physician Payment Review Commission

SADR – Standard Ambulatory Data Record

SAIAN – Survey of American Indians and Alaskan Natives

SES – Socioeconomic Status

SIDR – Standard Inpatient Data Record

SSN – Social Security Number

USPD – Uniformed Services Prescription Database

VA – Veteran's Administration

Chapter 2

Review of the Literature

2.1 Introduction

This chapter is a review of the literature relevant to this research. It covers six broad areas:

1. An overview of asthma as a disease including definition, epidemiology, etiology, impact within the Department of Defense, pathophysiology, diagnosis, severity and management;
2. An overview of clinical practice guidelines including definition, classification, history of, functions, role of evidence;
3. Discussion of the role of theory in guideline development;
4. Discussion of the role of guidelines in asthma therapy;
5. The Department of Defense model for guideline use; and
6. Review of guideline effectiveness on asthma outcomes.

2.2 Asthma

2.2.1 Asthma Definition

Asthma is a chronic inflammatory disease of the airways characterized by recurrent episodes of airflow obstruction that are usually reversible either spontaneously or with treatment.(21) Variable airflow and bronchial hyperresponsiveness to a variety of stimuli are hallmarks of the disease. Depending on the severity of airflow restriction, symptoms of asthma may include breathlessness, wheezing, chest tightness, and cough. Airway

obstruction can occur in the asthmatic for a variety of reasons. These include: stimuli and allergen-induced acute bronchoconstriction; airway edema; chronic mucus plug formation; and airway remodeling. Based on current knowledge, the National Heart, Lung, and Blood Institute has defined asthma in the following manner, "Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli."⁽³⁾

2.2.2 Epidemiology

2.2.2.1 Prevalence

Despite advances in knowledge regarding the pathophysiology and management of asthma, prevalence of asthma in the United States and the world has increased sharply in the past 20 years. It is not clear whether these changes reflect a true increase in asthma prevalence or whether there has been an increase in the reporting of the disease, due, at least in part, to changes that have occurred in the International Classification of Diseases (ICD).⁽²⁾ Nevertheless, asthma is estimated to affect about 15 million Americans, one-third of them children.⁽³⁾ Data from the National Health Interview Survey indicate that

the annual prevalence rate of asthma increased from 3.1 percent in 1980 to 5.4 percent in 1994.(19, 22) The latest data suggest the prevalence rate to now be as high as seven percent for all children in the United States.(23)

The prevalence of asthma varies among ethnic groups in the United States with higher prevalence being reported among the poor and minorities in urban settings.(24, 25) Using data from the NHANES II survey of 1976 to 1980, Gergen and colleagues reported the prevalence of asthma in African American and Caucasian children using a sample of 5,672 children, six months to eleven years of age. When defined by 'wheezing' and/or 'physician diagnosis' the prevalence of asthma among Caucasian children was lower than among African American children (6.2% versus 9.4% respectively, $p < 0.01$). When defined only by 'wheezing,' asthma prevalence declined in both groups but was still higher in the African American group (5% versus 7.3%, no p-value reported). Even after adjusting for other risk factors (gender, young maternal age, residence in a central city, and poverty), this study suggested the prevalence of asthma to be significantly higher among African American children than for Caucasian children (OR = 1.7; 95% CI: 1.2 to 2.1).(25)

Litonjua et al, in a cross-sectional study of the Boston Massachusetts area, reported a greater risk of asthma for both African Americans and Hispanic children as compared to white children (OR = 2.9; 95% CI: 1.0 to 8.0; and OR = 5.3; 95% CI: 1.6 to 17.5 respectively). When adjusted for socioeconomic status (SES) however, the risks

associated with African Americans and Hispanics were lowered in both groups (OR = 0.8; 95% CI: 0.2 to 3; and OR = 2.5; 95% CI: 0.5 to 11.7 respectively). Although the confidence intervals for these results were fairly wide and, in some instances, non-significant, the authors concluded that SES might play a role in the asthma prevalence differences between ethnic groups.(26) In contrast to the above studies however, Miller was unable to detect any difference in the rate of hospital admissions between African American and Caucasian children after adjusting for income using the 1988 and 1991 National Maternal and Infant Health Survey.(27)

The early literature reporting on asthma in the children of the Native American population suggested asthma prevalence in this group was somewhat lower than in the general US population. Herxheimer, reviewing records in the Indian Health System (IHS) facilities, discovered a number of cases of bronchial asthma, especially at the Phoenix Indian Medical Center, but concluded that there were strikingly few cases of asthma among Native Americans of the southwest and of the northern plains.(28) Similar results were reported by Slocum and coworkers who identified only one patient with asthma in 9,000 consecutive Native American visits to the IHS clinic at Lama Deer, Montana, between 1974 and 1975.(29)

Using combined data from the 1987 National Medical Expenditure Survey (NMES) and the 1987 Survey of American Indians and Alaska Natives (SAIAN), Stout and associates estimated the prevalence of asthma among 2288 American Indian and Alaska Native

(AI/AN) children ages one to 17 to be 7.06 percent (95% CI: 5.08 to 9.04). This was lower than the US estimate based on the NMES data for all children aged one to 17 of 8.4 percent (95% CI: 7.65 to 9.15).(30) A more recent study by Liu and associates suggests that the rate of asthma among children in the Native American population is increasing. They report that hospitalization rates for asthma and bronchiolitis doubled for AI/AN children between 1987 and 1996, whereas the general population saw increases of about 50 percent.(31) Another study of IHS hospitalizations reported AI/AN childhood asthma hospitalizations rates were comparable to those for Caucasian children.(32) If SES were a primary risk factor for asthma one would expect that prevalence would be higher in the AI/AN population than in the Caucasian population. However, this does not seem to be the case. Liu and her colleagues offer a possible explanation for this by hypothesizing that, unlike other ethnic groups that fall into a lower socioeconomic status, the AI/AN have improved access to health care through the IHS. Of additional interest in the findings of Liu et al was the fact that approximately 60 percent of the AI/AN asthma hospitalizations occurred in children living in urban ZIP code areas.(32)

2.2.2.2 Morbidity

Asthma is the third-leading cause of preventable hospitalizations in the United States.(18) Approximately 39 percent of potentially avoidable hospitalizations of children under 15 years old are due to asthma. Asthma accounts for 21 percent of potentially avoidable hospitalizations in patients 15 to 44 years old, and 15 percent of avoidable hospitalizations in patients 45 to 64 years old.(18) The primary factor contributing to the

increase in asthma morbidity (as well as mortality) appears to be undertreatment of asthma.(33) A survey of patients admitted to a Baltimore hospital with moderate to severe asthma reported that fewer than half had been prescribed inhaled anti-inflammatory therapy as recommended by the National Heart, Lung, and Blood Institute.(34) It has been suggested that undertreatment may be associated with factors such as: 1) lack of access to ongoing medical care; 2) inability to afford care; 3) cultural and language barriers; and 4) lack of patient education about the seriousness of asthma.(35, 36)

Hospitalization and morbidity rates appear to be associated with ethnicity. Clark et al reported hospitalization rates in nonwhites to be twice what they were for whites.(1) One study suggests that the rate to which asthma restricts normal daily activity was 30 percent more often for African Americans than for Caucasians.(19) Although not well understood, it appears that at least in part, these observed differences between ethnic groups might have a link to various socioeconomic factors.(37) Included in these factors is the probability that minority ethnic groups have higher levels of exposure to allergens such as environmental pollutants and tobacco smoke, a decreased access to medical care, and lower levels of financial and social support.(38)

2.2.2.3 Mortality

In addition to the recent increases in asthma prevalence, are reports of similar increases in the asthma mortality rate. From 1982 through 1991, the overall annual age-adjusted

death rate for asthma in the US increased by 40 percent - from 3154 deaths to 5106 deaths a year and the rate among children and young adults was even higher. Clark et al reported an increase in childhood asthma mortality of nearly 80 percent between the years of 1980 and 1993.(1) For the same time period, the Centers for Disease Control (CDC) reported the annual age-specific asthma rate for persons up to 24 years of age to have increased by 118 percent to 3.7 cases per million population.(23) As with prevalence, asthma mortality appeared to be associated with an urban environment. In a study of the geographic variation associated with US asthma deaths, Weiss and Wagener reported the two highest death rates were in urban centers. The death rate attributable to asthma was twice in Cook County, Illinois (Chicago), and three times in New York City, what it was on average for the whole United States.(39) As further illustration of the disparity between the rural and urban asthma mortality rate, Carr and associates reported that for 1986, approximately six percent of all asthma related hospitalizations, and seven percent of asthma related deaths in the United States, occurred in New York City - a city that at that time represented only three percent of the nation's population.(40) Furthermore, for the years between 1980 and 1988, Marder et al reported the annual asthma mortality rate for persons aged 5 to 34 years living in Chicago, to be 16.4 deaths per million - approximately three times the US rate.(41) Other urban areas reported to be associated with high asthma mortality included Maricopa County, Arizona, and Fresno County, California.(42)

Similarly to urbanicity, ethnicity has also been associated with asthma mortality. Grant et al., using mortality data obtained from the National Center for Health Statistics for the years between 1991 and 1996, reported asthma standard mortality ratios (SMRs) that were significantly higher for African Americans than for Caucasians (SMR = 3.34 versus 0.65, $p < 0.001$), suggesting an independent association between race/ethnicity and asthma mortality even after controlling for SES.(43) Two other studies reported an association between race/ethnicity and asthma mortality/morbidity. In a review of all deaths attributable to asthma in Chicago between 1980 and 1988, Marder et al reported 82.9 percent occurred among African Americans.(41) Similarly, a study conducted in Maryland reported that hospital discharge rates were disparately higher for African American children (3.75/1,000) than for Caucasian children (1.25/1000).(42)

Although not clearly understood, there appears to be conflicting evidence regarding the effect of gender on both asthma prevalence and mortality. Sears et al, who were studying a birth cohort through 13 years of age, reported that boys were 1.6 times more likely to be diagnosed with 'current' asthma and 1.4 times more likely to have 'ever-diagnosed' asthma, than girls.(44) Wieringa et al. reported similar findings in a cross-sectional survey of 6432 children aged six to seven years and 2864 children 13 to 14 years old.(45) The prevalence rates of respiratory and nasal symptoms and a diagnosis of asthma and hay fever were higher in six to seven year old boys than in girls (OR = 1.07 to 3.04). The occurrence of asthma in the 13 to 14 year old group was also higher for boys than for girls. In another longitudinal cohort study, Sherman et al. reported the relative risk of

asthma associated with the male gender in children between five and seven years of age to be 2.39 (95% CI: 1.35 to 4.23).(46) Several other studies investigating the risk factors for childhood asthma have reported similar results.(47, 48) In a recently published study in which the association of obesity and asthma were studied together, Castro-Rodríguez and colleagues reported that females, but not males, who were overweight or obese at ages eleven and thirteen, were more likely to have current wheezing at ages eleven and thirteen but not at ages six or eight. This effect was strongest among females beginning puberty before the age of eleven. Females who became overweight or obese between six and eleven years of age were seven times more likely to develop new asthma symptoms at age eleven or 13 ($p = 0.0002$). (49) A study of a population of school aged children (13 to 14 years) in Costa Rica, a country with one of the highest childhood asthma rates in the world (23.7% current wheezing) reported no difference in asthma rates based on gender.(50) In a study of deaths due to asthma in Washington State, females and males were reported to have similar mortality rates through 1980. By 1989, the female rate increased to 2.25, nearly 1.66 times greater than the male rate of 1.38. This was an increase of 31 percent for female rates and a decrease of 17 percent for male rates.(51) In yet another study investigating the role of gender on asthma hospital admissions, it was reported that although there was no apparent difference in asthma prevalence based on gender, women had a considerably higher risk ($RR=1.7$, 95% CI: 1.2 to 2.4) than men of being admitted to a hospital for the disease.(52)

2.2.3 Etiology

Epidemiologic studies support the notion that atopy, or the genetic predisposition for developing an IgE-mediated response to an allergen, is the most identifiable predisposing factor for asthma.(53) Studies conducted among 'twins' provide the most compelling evidence and suggest that up to 50 percent of a person's susceptibility to asthma might be accounted for by genetic factors.(54) Other potential links to the development of asthma include infectious, allergenic, environmental, socioeconomic, and psychological factors.(55) Potential precipitating factors of asthma are presented in Table 2.1.

Table 2.1: Potential Precipitating Factors of Asthma

<i>Precipitating Factor</i>	<i>Specific agents or events</i>
Respiratory Infection	Respiratory syncytial virus (RSV), rhinovirus, influenza, parainfluenza, <i>Mycoplasma pneumonia</i>
Allergens	Airborne pollens (grass, trees, weeds), house-dust mites, animal danders, cockroaches, fungal spores
Environment	Cold air, fog, ozone, sulfur dioxide, nitrogen dioxide, tobacco smoke, wood smoke
Emotions	Anxiety, stress, laughter
Exercise	Particularly in cold, dry climate
Drugs/preservatives	Aspirin, NSAIDs (cyclooxygenase inhibitors), sulfites, benzalkonium chloride, β -blockers
Occupational stimuli	Bakers (flour dust); farmers (hay mold); spice and enzyme workers; printers (arabic gum); chemical workers (azo dyes, anthraquinone, ethylenediamine, toluene diisocyanates, polyvinyl chloride); plastics, rubber, and wood workers (formaldehyde, western cedar, dimethylethanolamine, anhydrides)

(Adapted from Kelly HW, Kamada AK. Asthma in : DiPiro J, Yee GC, Talbert RL, Hays PE, Matzke GR, Posey LM, editors. Pharmacotherapy: A Pathophysiological Approach. Stamford, CT: Appleton & Lange; 1999)

2.2.4 Pathophysiology

Airflow limitation is the hallmark of asthma. It is recurrent and can be caused by a variety of changes in the airway. Exaggerated bronchoconstriction is one source of airflow limitation. The pathogenesis of airway hyperresponsiveness seen in asthma appears to be associated with the inflammatory response with the airways that can lead to the clinical symptoms of wheezing and dyspnea after exposure to allergens, environmental irritants, viral infections, cold air, or exercise.(3, 56) Factors contributing to airway inflammation in asthma are multiple and involve complex interactions among inflammatory cells, cell mediators, and normal cells of the airways.(57) The immunohistopathologic features of asthma include denudation of the airway epithelium, collagen deposition beneath the basement membrane, edema of the airway mucosa, mast cell activation, and inflammatory cell infiltration with neutrophils, eosinophils, and lymphocytes.(53) Current thought is that the inflammatory process of asthma occurs in two stages. The first stage occurs as a result of a precipitating event or trigger that causes the release of inflammatory mediators from bronchial mast cells, macrophages, T-lymphocytes, and epithelial cells. These substances direct the migration and activation of other inflammatory cells, such as eosinophils and neutrophils, to the airway where they cause injury such as alterations in epithelial integrity, abnormalities in autonomic neural control of airway tone, mucus hypersecretion, change in mucociliary function, and increased airway smooth muscle responsiveness.(3) The net effect of these activities is a narrowing of the airway leading to asthma symptoms such as nighttime cough, wheezing, difficulty in breathing, chest tightness, and disturbances in sleep.(1) The second stage of

inflammation generally occurs four to eight hours after the initial stage. It is characterized by persistent airflow obstruction, airway inflammation, and bronchial hyper-responsiveness associated with the slow-reacting substance (SRS) of anaphylaxis.(21)

Asthmatic airflow restriction can also occur independent of smooth muscle contraction or bronchoconstriction through airway wall edema. Increased microvascular permeability and leakage caused by released mediators can contribute to mucosal thickening and swelling of the airway. Other complications that can occur as a result of the pathophysiological process are airway obstructions due to the formation of mucous plugs and airway remodeling. Both of these conditions are characteristic of more advanced, intractable forms of asthma, in which airflow limitation can become persistent. (3)

2.2.5 Diagnosis

The diagnosis of asthma often requires the use of clinical judgment on the part of the practitioner. This is because the signs and symptoms of asthma can vary widely from one patient to another as well as between asthmatic episodes in the same patient. To establish a diagnosis of asthma, the NHLBI guidelines suggest that: episodic symptoms of airflow obstruction are present; airflow obstruction is at least partially reversible; and alternate diagnoses are excluded.(3) Additionally, the NHLBI asthma guidelines suggest the use of the following techniques for making a positive asthma diagnosis: (1) a detailed medical history; (2) a physical exam focusing on the upper respiratory tract, chest, and

skin; and (3) spirometry.(3) The primary purpose of spirometry is to assess the degree and reversibility of airflow obstruction.

2.2.6 Asthma within the United States Department of Defense

There is a long history between the US military and asthma. One of the earliest and more prominent military members documented with asthma was the Union Civil War General, William Tecumseh Sherman.(58) Although his asthma never appeared to interfere with his military duties, his struggles with it were reported to be so constant that one biographer referred to it as “his lifelong enemy.”(59)

In today’s military environment, the impact of asthma is evident in several ways. First, it is a readiness issue for active duty and reserve military troops and has long been considered a reason for disqualification from military service.(6)

Of the 30 percent of applicants that were disqualified for military service in World War II, two percent of them were for asthma.(7) Before 1995, the U.S. Department of Defense (DoD) allowed individuals with a history of asthma symptoms that ceased by age 12 to enter the military. This was changed in 1995 such that a reliable diagnosis of asthma at any age would be enough to disqualify an individual from military service. This directive turned out not to be iron clad as individuals with asthma found it still possible to gain entrance into the military by obtaining a medical waiver. The waiver authorities could grant a medical waiver on an individual basis by taking into consideration a number of factors including such things as the absence of asthma

symptoms since the age of 12 years, successful participation in high school athletics (without asthma symptoms), and evidence of high motivation.(7)

The impact of asthma on troop readiness was evident in the early 1990's with the inability to deploy over 500 U.S. Army soldiers with an asthma diagnosis to Operation Desert Storm, and the evacuation of more than 200 others already deployed.(6)

Published estimates of asthma prevalence in the US military range from a low of less than one percent in military members assigned to submarine duty, to a high of six percent in a study reporting exercise-induced airflow obstruction in US Air Force members.(9,10)

Apart from the recruitment, eligibility, and treatment issues of asthma in the active duty force, the military health service (MHS) also has health care responsibilities for those in the dependent and retiree sectors of the DoD population. In fact, according to one report, dependents and retirees make up close to 80 percent of the eligible population served by the MHS.(11) The health care issues of this population range widely from the pre- and perinatal needs of young mothers and infants to the needs associated with the aging DoD population.(12) Included in these issues are the concerns of chronic conditions such as asthma.

2.2.7 Classification of Asthma Severity

The NHLBI asthma guidelines classify asthma severity into four categories based on the following factors: symptom frequency and severity; occurrence of nighttime symptoms;

and, volume and variability of the pulmonary function tests. The NHLBI asthma classification system is presented in Table 2.2.

2.2.8 Management of Asthma

Effective management of asthma requires both pharmacologic and nonpharmacologic components.(6) The NHLBI guidelines suggest that level of patient motivation and disease knowledge also have an effect on outcomes. Because of the fluctuating nature of asthma symptoms, the ability of a patient to self-manage the disease is critical. Self-management skills include knowledge of the disease pathophysiology, the appropriate use of medications, the ability to recognize triggers, and the ability to recognize early signs of disease deterioration.

According to Kelly and associates, self-management skills can be effectively acquired when the patient and health care team agree to work together in a partnership. Various members of the health team provide education and training to the patient, and in return, the patient makes a reasonable commitment to compliance.(56)

The two primary goals of pharmacologic therapy for asthma are long-term control and relief of acute symptoms or exacerbations.(56) With growing evidence establishing inflammation as the major contributor to the pathogenesis of asthma, anti-inflammatory treatment has become the pharmacologic treatment of choice for long-term control.(3) For relief of acute symptoms and exacerbations, short-acting β -agonist bronchodilators

are the preferred therapy.(3) A list of selected control and quick-relief agents, along with their respective indications, is provided in Appendix A.

Table 2.2: Classification of Asthma Severity

	<i>Symptoms</i>	<i>Nighttime Symptoms</i>	<i>Lung Function</i>
Step 4 Severe Persistent	Continual symptoms Limited physical activity Frequent exacerbations	Frequent	FEV ₁ or PEF \leq 60% predicted
Step 3 Moderate Persistent	- Daily symptoms - β_2 – agonist needed daily - Exacerbations affect activity - Exacerbations \geq 2 times a week; may last days	> 1 time a week	- FEV ₁ or PEF > 60% to < 80% predicted - PEF variability > 30%
Step 2 Mild Persistent	- Symptoms > 2 times a week but < 1 time a day - Exacerbations may affect activity	> 2 times a month	- FEV ₁ or PEF \geq 80% predicted - PEF variability < 20%
Step 1 Mild Intermittent	- Symptoms \leq times a week - Asymptomatic and normal PEF between exacerbations	\leq times a month	- FEV ₁ or PEF \geq 80% predicted - PEF variability < 20%

(Adapted from National Heart, Lung and Blood Institute: Guidelines for the Diagnosis and Management of Asthma. NIH Publication No. 98-4051, Rockville, MD: NIH Publishers, May 1997.)

2.2.8.1 Stepwise Approach to Management of Chronic Asthma

The goal of asthma therapy is to maintain control of asthma with the least amount of medication possible and, thereby, reducing the risks of adverse effects. Because of the chronicity of the disease and the rapid changes that can occur in severity and symptoms, this goal is best addressed with a medication plan that is easily adjusted. The NHLBI asthma guidelines 'Stepwise Approach' achieves this type of flexibility.(3) This approach allows for either an increase or decrease in medication dose, frequency of

administration, or both, depending upon the observed severity of disease. The main elements of this approach (for adults) are outlined in Table 2.3.

Table 2.3: Stepwise Approach to Managing Asthma

Adults & Children > 5	Long-term Daily Meds	Quick Relief
Step 4 Severe Persistent	-Anti-inflammatory: High Dose ICS and -LAB and OCS	- SIB as needed for symptoms - Vary treatments based on severity - ↑ SIB use on daily basis indicates need for additional control therapy
Step 3 Moderate Persistent	-Anti-inflammatory: Medium dose ICS or -Low dose ICS and LAB - If needed: ICS and LAB	- SIB as needed for symptoms - Vary treatments based on severity - ↑ SIB use on daily basis indicates need for additional control therapy
Step 2 Mild Persistent	- Anti-inflammatory: Low dose ICS or cromolyn or nedocromil - Sustained-release theophylline or Leukotrienes	- SIB as needed for symptoms - Vary treatments based on severity - ↑ SIB use on daily basis indicates need for additional control therapy
Step 1 Mild Intermittent	No daily medication needed	- SIB as needed for symptoms - Vary treatments based on severity - ↑ SIB use on daily basis indicates need for additional control therapy
Stepwise adjustments	Step Down: Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible	Step Up: If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control (avoidance of allergens or other factors that contribute to asthma severity

ICS – Inhaled Corticosteroids, OCS – Oral Corticosteroids (tab/syrup) SIB – Short-acting Inhaled Bronchodilator, SAB – Short-acting Oral Bronchodilator, LAB – Long-acting Bronchodilator (inhaled or oral) (Adapted from National Heart, Lung and Blood Institute: Guidelines for the Diagnosis and Management of Asthma. NIH Publication No. 98-4051, Rockville, MD: NIH Publishers, May 1997.)

2.2.8.2 Management of Asthma Exacerbations

Asthma exacerbations are acute or subacute episodes of progressively worsening shortness of breath, cough, wheezing, and chest tightness, or some combination of these symptoms. They are characterized by decreases in expiratory airflow that can be documented and quantified by simple measurement of lung function.(3) Early treatment is the best strategy for management of asthma exacerbations. The following elements have been recognized as important to the treatment process:

- a written action plan to guide in self-management
- early recognition of exacerbation, including worsening FEV₁ or PEF.
- prompt communication with provider regarding deterioration in symptoms or decreased effectiveness of medications.
- Appropriate intensification of therapy according to self-management action plan.
- Removal of or withdrawal from allergic or irritant precipitants in the environment that may be contributing to the exacerbation.

The primary treatment goals for asthma exacerbations include the correction of significant hypoxemia and the rapid reversal of airflow obstruction. The administration of oxygen is often useful in reversing hypoxemia and the repetitive or continuous use of inhaled beta₂-agonists is the treatment of choice for reversing airflow obstruction. (3)

2.2.9 Economic Burden of Asthma

The costs associated with health care use and disabilities attributed to asthma are reflective of the increasing prevalence of the disease.(60) Although there is some

disparity in the literature between the estimates, there is no disagreement to the fact that the economic burden of asthma is increasing. According to Drummond, costs associated with a disease treatment can be one of four types.(61) Direct medical costs are resources spent on medical services or products as a direct consequence of a disease of illness; direct nonmedical costs are expenditures related to the provision of medical care, but incurred outside the medical sector such as transportation to and from a hospital; indirect costs are the amounts spent or lost as an indirect consequence of illness or consumption of medical care such as lost wages or a decrease in productivity; and intangible costs are those that associated with pain and suffering and social and emotional functioning.(62) Table 2.4, adapted from Barnes et. al, provides several examples of each of these costs as they apply to asthma.(63) Using the National Medical Expenditure Survey (NMES), Smith et al estimated the total cost of asthma in 1987 to be \$5.8 billion (1994 dollars). Direct costs represented the majority (88%) of the total, with indirect costs comprising the remainder.(64) Weiss and his coworkers estimated the burden of asthma to be approximately \$6.2 billion in 1990, and then to have increased to \$10.7 billion in 1994.(4, 65) The most recent report by Weiss (1998) estimated the annual cost of asthma to have exceeded \$12.5 billion.(5)

Using the NMES survey, Lozano and coworkers (1987) compared the health care resources used between asthmatic and non-asthmatic children. The results suggested a much higher rate of resource consumption among children with asthma than for those without asthma. Utilization rates for prescriptions, ambulatory provider visits, and

emergency department visits were 3.1, 1.9, and 2.2 times greater, respectively, for asthmatic children than they were for non-asthmatic children (no p-values reported).(66)

Table 2.4: Types of Costs Associated with Asthma

<i>Direct Medical Costs (resources consumed)</i>	<i>Direct Nonmedical Costs (resources consumed)</i>	<i>Indirect Costs (resources lost)</i>	<i>Intangible cost (Quality of Life)*</i>
Cost of doctors'/nurses' time	Transportation costs associated with treatments	Loss of productive work by patient	Grief
Cost of social support (e.g. home help)	Lodging costs associated with treatments	Loss of productive work by patient's family and friends (e.g. mother taking time off work to care for child with asthma)	Fear
Cost of medications	Telephone charges associated with therapy	Loss of productive work due to patient's early retirement or premature death	Pain
Cost of hospital treatment		School days lost	Unhappiness
Cost of disposable equipment		Restricted activity	
Capital cost of land, buildings, equipment			

*All of these apply not only to the patient but also to his/her friends and family
(Adapted from Barnes PJ et al. The Cost of Asthma. *European Respiratory Journal* 1996;9:636-642.)

In another study, Serra-Batlles et al. reported that the average cost of treating asthma in Spain varied according to the degree of disease severity. Reporting in US dollars, the annual cost was found to be highest for those with severe asthma (\$6,393), less for those with moderately severe asthma (\$2,407), and even less for those with mild asthma

(\$1,336). The average annual cost of treatment for all asthma was \$2,879 per patient.(67) These findings suggested that even if unable to prevent the occurrence of asthma, the ability to control disease severity would have the potential to produce cost savings at both the individual and health system levels.

Indirect costs are also an issue with calculating the impact of asthma. Using data from the National Institutes of Health, Massanari (2000) estimated that asthma accounts for more than 10 million school days lost annually in the US – more than any other chronic disease.(2) Further, a study published in 1994 reported the amount of restricted activity caused by asthma to be in excess of 100 million days annually. The report went on to state that the annual cost of lost productivity, due to asthma related worker absenteeism, was close to \$1 billion.(4)

2.3 Guidelines Development

2.3.1 Guideline Definition

Guidelines have been described in a number of different ways. Webster's *New World College Dictionary* defines a guideline as "a standard or principle by which to make a judgment or determine a policy or course of action".(68) Heffner defines guidelines to be statements made on the part of professional societies to identify best current practices of care, or ways to educate physicians and improve health care.(69) Similarly, Woolf refers to guidelines as "official statements or policies of major organizations and agencies on proper indications for performing a procedure or treatment of the proper management for

specific clinical problems".(70) In the context of health care delivery perhaps the most widely quoted definition is the one developed by the Institute of Medicine (IOM). This definition simply states that guidelines are: "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances".(71) According to Berger, these 'statements' can be used to describe preferable courses of clinical action, ranges of acceptable medical practice, required clinical responses, or a combination of these actions with applications to prevention, diagnosis, treatment and/or palliation strategies.(72) Grimshaw and Russell add that guidelines expound appropriate management options for symptom clusters, conditions, or procedures with the principal aim of promoting good performance.(73) Although not universally interchangeable, terms that have periodically been used in the scientific literature to convey the same meaning as guidelines include "standards", "recommendations", "protocols", "policies", "algorithms", "consensus conferences of statements", and, more recently, "practice parameters", "clinical pathways", and "practice options."(70, 72) Dolter would suggest there are fine nuances between these terminology. For instance, she defines Clinical Practice Guidelines (CPGs) as statements that describe the 'right THING to do' whereas Clinical Pathways are defined as statements describing the 'right WAY to do the right THING.'(74) Regardless of the terminology used, Curry argues that succinct and credible practice guidelines can be useful in reducing the burden on individual practitioners to synthesize and organize evidence-based knowledge across a wide range of medical conditions. He further states that guidelines can help define the roles and responsibilities of all practice-team members

more clearly, resulting in greater efficiency and higher quality of care.(75) Over the past 20 years the use of guidelines in health care delivery has increased dramatically. In the United States alone there are at least 2,000 guidelines in use in a variety of health care settings.(76) A MEDLINE search conducted in 2000 listed 4,127 publications since 1966 under the category *practice guideline*, 3,969 of which were published since 1989.(77)

2.3.2 Guideline Classification

Important to the guideline development process is who develops them. They can be developed by an *internal* group comprised of clinicians who are going to use them; an *intermediate* group comprised of representatives of the clinicians who are going to use them; or an *external* group in which the using clinicians are excluded.(73) According to Grimshaw and Russell, guidelines developed by an *external* group are more likely to be scientifically based, while those developed by an *internal* group have the greatest likelihood of being used.(78) Additionally, guidelines can be classified according to the analytical processes used in their development. Grimshaw and Russell describe three separate categories of guideline development– *informal consensus*, *formal consensus*, and *evidence-linked guideline* development.(73) Each of these methods is briefly discussed below.

2.3.2.1 Informal Consensus Guideline

Guidelines that emerge from meetings of expert panels in which agreement is reached through open discussion are called informal consensus guidelines. Specialty societies,

federal agencies, and task forces have used this method for decades. In many instances, recommendations, or the guidelines themselves, are produced in a single meeting. According to Woolf, informal consensus remains the most common approach to developing a practice guideline. The main appeal of this approach is that it is relatively easy, fast, and free of complex analytic procedures.⁽⁷⁹⁾ In addition, panel members who are unfamiliar with formal analytic methods find it easy to adopt.⁽⁷³⁾

The main disadvantage to the informal consensus approach is the potential for low quality guidelines. This can occur for several reasons. First, there are fundamental limitations to the validity of expert opinion as a basis for defining appropriateness – because a group of individuals think a practice is beneficial doesn't necessarily make it so. Second, with no explicit methods for achieving consensus, questions may arise as to how consensus was reached. Guidelines developed in group meetings without systematic procedures can be influenced by such things as group dynamics, dominant and outspoken personalities, and organizational and specialty politics. Third, readers have a difficult time judging the scientific merits of a guideline in the absence of documented methods.⁽⁷⁹⁾

2.3.2.2 Formal Consensus Guideline

Similar to the informal consensus process, guidelines developed using the formal consensus process are also driven by expert opinion. The primary difference between the two methods is that the formal method is a more extended and rigorous process. An

example of this approach is the consensus program used by The National Institutes of Health. It consists of a structured two and a half day conference during which time an expert panel discusses, arrives at consensus, and makes recommendations on a specified subject. In this way, recommendations on more than 80 topics have been developed over the course of 15 years.(80) Other organizations that have used the formal consensus approach to guideline development include the American Medical Association and the RAND corporation.(81, 82) Although this process provides greater structure to the analytic process than does the informal consensus process, the absence of explicit criteria and the requirement to produce recommendations quickly in a single meeting have been criticized.(83)

2.3.2.3 Evidence-Based Guideline

The hallmark of evidence-based guidelines is the incorporation of research derived evidence into the final recommendations. Unlike informal and formal consensus guideline development, evidence-based guidelines depend upon the systematic review of the literature, appropriately adapted to local circumstances and values.(84) The linkage between recommendations and supporting evidence is often accompanied by a scoring system that allows the reader to judge the quality of the supporting evidence.(85)

Although this approach to guideline development has been credited with enhancing the scientific rigor of practice guideline development, it is not without its own set of criticisms. Woolf states that evidence-based guidelines are often unable to respond to recommendation needs in the absence of clear evidence. He goes on to argue that since

only a small proportion of current interventions have been validated through clinical studies, a strict adherence to this method of guideline development would exclude guideline use in most of modern medical practice.(79)

2.3.2.4 Common Characteristics of Guidelines

Regardless of how they are developed, there are characteristics common to all guidelines.

First, according to Eddy, guidelines are composed of elements, describing different aspects of the patient's condition and the care to be given.(86) Irvine and Donaldson classify elements into one of three categories based on the quality of evidence used in their development. Elements that are well founded scientifically and have important implications for patient outcomes are classified as '*mandatory*.' Those for which the scientific evidence is somewhat less convincing are classified as '*near mandatory*,' and elements which have alternative management strategies, but no scientific evidence about relative effectiveness, are classified as '*optional*.'(87) Second, guidelines can either be deterministic or branching in structure. Deterministic guidelines comprise a fixed list of elements to be followed, irrespective of the information available to the provider. Branching guidelines, on the other hand, allow alternate courses of action to be followed depending upon the available information. Deterministic guidelines, although useful in defining a minimum levels of care, tend to ignore the deductive nature of medical decision-making in clinical settings, and are thus seldom used. A common method for presenting branching guidelines is in the form of either an algorithm or flowchart.(87)

2.3.2.5 Assumptions

According to Field and Lohr, there are six assumptions upon which guideline use is dependent.⁽⁷¹⁾ They are:

1. A sufficient quantity and quality of scientific evidence exists to serve as a foundation for guidelines.
2. Programs to develop guidelines will be organized, funded, and effectively managed to produce a considerable volume of valid, usable statements about appropriate care for clinically and financially significant health conditions or technologies.
3. Substantial numbers of clinicians, patients, and others will have the opportunity, the support, and the incentives to read, understand, accept, and use these statements in ways that change patterns of clinical practice, health behavior, or payment for health care services in desired directions.
4. Such changes will be broad and intense enough to improve health outcomes.
5. On balance, the entire body of guidelines as actually developed and used will lead to more cost controlling than cost-increasing behavior on the part of providers and patients.
6. The body of guidelines will continually expand to cover new areas so that net rates of increase in health care costs and absolute levels of expenditures will be lower than they would otherwise be.

2.3.3 Guideline Initiatives

2.3.3.1 Overview

Guideline use in health care is not new. Professional organizations, both public and private, have been developing guidelines for at least a half of century. The American

Academy of Pediatrics began publishing guidelines for the management of infectious diseases in 1938. The American College of Obstetricians and Gynecologists and American College of Physicians issued its first practice standards in 1959.(88, 89)

Significant early accomplishments in the area of guideline research include the joint effort between the American College of Cardiology and the American Heart Association in the development of guidelines for coronary artery bypass procedures, and the combined effort of the American College of Nuclear Physician and the Society of Nuclear Medicine in developing guidelines for nuclear medicine practitioners.(71)

Formal procedures for development of consensus guideline recommendations were first established in the 1970s at the National Institutes of Health (NIH) consensus development conferences. The appearance of evidence-based guidelines occurred simultaneously, a decade later in the 1980s, with the evolution of evidence-based medicine.(90, 91) The surge of guideline activity that has occurred over the last two decades is, in part, a result of certain activities undertaken by the Council of Medical Specialty Societies (CMSS), and the Congressional Physician Payment Review Commission (PPRC).(92) The 1988 PPRC conference provided a national focus on guidelines by emphasizing their use as a vehicle for rationing and controlling health care expenditures.(70) This along with recommendations made by the Omnibus Budget Reconciliation Act of 1989 (OBRA 89) for periodic review and updating of 'clinically

relevant guidelines,' helped to establish guidelines as a useful and acceptable way of providing health care services.(71)

2.3.3.2 Government Role in Guideline Development

Government support for practice guidelines has occurred primarily in the federal domain, although some states, such as California, have developed guideline initiatives of their own. The three distinctive roles of the federal government in guideline development include: 1) directly convening and managing groups to develop practice guidelines; 2) funding the development of guidelines by other groups; and, 3) funding and conducting basic and applied research to strengthen the clinical knowledge base and the methodologic tools that support better guideline development.(71)

The U.S. Congress formalized government involvement in guideline development in 1989 with the creation, within the U.S. Public Health Service, of the Agency for Health Care Policy and Research (AHCPR). Under the terms of Public Law 101-239, this agency was given broad responsibilities for supporting research, data development, and other activities that would enhance the quality, appropriateness, and effectiveness of health care services.(93) As one of its initiatives, AHCPR requested advice from the Institute of Medicine (IOM) on how to foster joint public-private research to develop, disseminate, and evaluate guidelines for clinical practice under the sponsorship of the agency's Forum for Quality and Effectiveness in Health Care.(85) An agreement reached between the AHCPR and IOM resulted in the appointment of a multidisciplinary

committee responsible to provide oversight and technical assistance in the area of guideline development. The end result was the publication of two seminal works:

Clinical Practice Guidelines: Directions for a New Program, published in 1990; and *Guidelines for Clinical Practice: From Development to Use*, published in 1992.(93,71)

Other federal agencies with interest and responsibilities related to practice guidelines include the Food and Drug Administration (FDA), National Institutes of Health (NIH), Centers for Disease Control (CDC), the U.S. Preventive Services Task Force, the Health Care Financing Administration (HCFA) along with its contracting carriers, fiscal intermediaries, and peer review organizations; and more recently the medical services within the Department of Defense (DoD).

2.3.3.3 Private Sector Medical Groups

Among providers of health care in the private sector, medical groups have been involved with guideline initiatives for a number of years. Examples include the American College of Physicians Clinical Efficacy Assessment Project, established in 1980, and the Joint American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures.

2.3.3.4 Medical Societies

Medical society involvement in guideline development increased dramatically in recent years. According to a 1994 survey by the American Medical Association (AMA), over

50 physician organizations and national medical specialty societies had developed some form of practice guidelines. This represented a considerable increase over the results of a similar survey conducted a decade earlier, in which only eight societies had reported involvement in guideline development.(94) Organizations now using guidelines included general societies such as the AMA, the American Academy of Family Physicians, the American College of Cardiology, the American College of Physicians, and the American Society of Anesthesiologists. These organizations often used their peer-reviewed journals as an authoritative method of integrating guideline recommendations into medical care.(94)

2.3.3.5 Research Organizations

Among independent research organizations, the RAND Corporation and the Institute of Medicine (IOM) have done considerable work in the area of guideline research and development. Both have worked collaboratively with government and private organizations such as the Academic Medical Center Consortium (AMCC), AMA, and the AHCPR and the DoD.

2.3.3.6 Academic Centers

Interest in guideline development has also occurred among academic centers. This has primarily been driven by the perception that guidelines developed by government, organized medicine, payers, or other groups with financial or other interests in the final product, could be influenced by bias. In 1989, nine academic medical centers with strong

interests in practice guidelines founded the Academic Medical Center Consortium (AMCC). The Clinical Appropriateness Initiative was a formal collaboration between the AMCC, the AMA, and the RAND Corporation to develop practice guidelines and to evaluate their impact on practice behavior.(70)

2.3.3.7 Insurance Industry

Another sector of the health care industry involved in guideline development is the health insurance industry. Historically, the purpose and use of guidelines in this industry were for making claims decisions and utilization assessments. One of the leaders of guideline use in the insurance industry was Blue Cross/Blue Shield (BCBS). Since the mid 1970s they collaborated with physician groups, including the American College of Physicians, to develop guidelines for use in the adjudication of physician claims.(70) Of the group and staff model HMOs that have developed guidelines, those developed by the Harvard Community Health Plan have been recognized as being particularly noteworthy.(95)

2.3.3.8 Employer Groups

Closely associated to the insurance industry are employer groups which form powerful purchasing coalitions. The purpose of these coalitions is to develop purchasing alliances that can negotiate health care benefits on behalf of member companies through the combination of economic incentives and systems of accountability.(96) In 1995, over 8,000 employers belonged to an employer health coalition.(97) Two of the most active and influential coalitions are those in California and Minnesota. California's Pacific

Business Group on Health (PBGH) was one of the largest, representing in 1994 over 30 major employers and 2.5 million persons. It used the collective-purchasing strategy with great success, achieving premium reductions of over ten percent from some of the organizations.(97) Part of the success of these groups is due to the incorporation of guideline use into their systems of accountability. Health care plans that want a share of health care dollars held by employer groups understand that they will be paid for performance that is consistent with established guidelines.(96) In 1996, over two million dollars from participating health care plans was retained by PBGH in the form of penalties, for not meeting the performance requirements of its guidelines.(98)

2.3.4 Guideline Functions

While the original intent of guidelines was to improve the quality of health care services provided in this country, Berger and Rosner suggest this is no longer the only reason for their use.(99) Additional reasons cited in the literature include the ability to increase health care efficiency, decrease costs, reduce liability, provide medical education, assist in utilization review and quality assurance activities, help in determining physician suitability for employment, and determining legal standards of care.(72) According to a 1990 report to Congress by the Committee to Advise the Public Health Service on Clinical Practice Guidelines, the five major functions of guidelines are: (1) assisting clinical decision making by patients and practitioners; (2) educating individuals or groups; (3) assessing and assuring the quality of care; (4) guiding allocation of resources for health care; and (5) reducing the risk of legal liability for negligent care.(93) Several

Several suggestions have been offered to explain the recent surge in guideline use. These include their ability to control for differences in patient care and physician practice due geographic variations,(100, 101) to respond to reports of significant rates of inappropriate care,(70) and to manage exploding health care costs.(102)

A partial list of guideline uses in health care is provided in Table 2.5

Table 2.5: Selected Uses of Guidelines Found in Health Care Literature

<i>Use of Guideline</i>	<i>Primary Guideline User</i>	<i>Reference</i>
Assisting in clinical decision making	Physicians Patients	Field & Lohr(93)
Educating individuals or groups	Providers Patients Administrators Policy Makers	Field & Lohr(93)
Guiding allocation or resources for health care	Providers Administrators Policy Makers	Field & Lohr(93)
Rationing of health care resources	Administrators Policy Makers	Loewy(99)
Cost Containment	Administrators Policy Makers	Gevers(103)
Reducing the risk of legal liability	Providers Administrators Policy Makers	Field & Lohr(93)
Improve efficiency of health care resources	Providers Administrators Policy Makers	Grimshaw & Russell(104)
Reducing inappropriate practice	Providers Patients Policy Makers Administrators	Field & Lohr(93)
Minimize medical errors	Providers Patients Policy Makers	Gross, Greenfield, et al(105)
Reduce geographic variation in care	Policy Makers Providers	Gross, Greenfield, et al (105)
Assist in utilization review	Administrators Policy Makers	Berger & Rosner(72)
Determining physician suitability for employment	Administrators	Berger & Rosner (72)
Policy enforcement	Administrators	Berger & Rosner (72)
Peer review processes	Physicians Administrators	Berger & Rosner (72)

2.3.5 Principles of Evidence-Based Research

Evidence-based medicine (EMB) is a major influence in the development of evidence-based guidelines, and calls for clinicians to make patient care decisions that are conscientious, explicit, and based on the judicious use of current best evidence.(106)

John M. Eisenberg, Director of the Agency for Healthcare Research and Quality, summarizes the principles of evidence-based medicine:(107)

- Demand high levels of evidence at all decision-making points.
- Question the validity, applicability of evidence to the circumstances. What works in one case may not be relevant to another.
- Understand that the lack of evidence that a treatment is effective is not the same as evidence that it is ineffective.
- Harness the power of information technology. This applies not only to improving the delivery of evidence-based medicine, but also for using it to improve collection, storage and retrieval of related data.
- Borrow from successful industries.
- Improve clinician-patient communication. Patients and providers must speak the same language.

2.4 Guideline Theory

2.4.1 Definition and Characteristics of 'Theory'

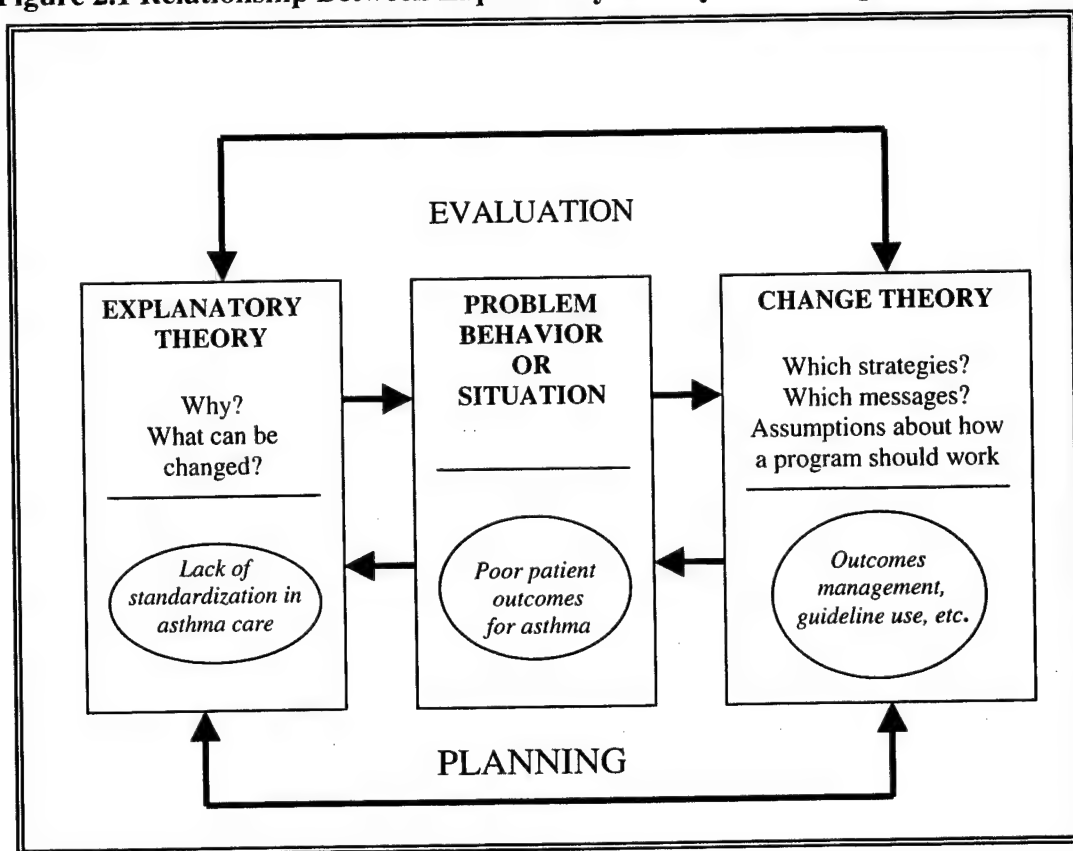
Theory has been defined as a set of interrelated concepts, definitions, and propositions that present a systematic view of events or situations by specifying relations among variables, in order to explain and predict the events or situations.(108) According to van Ryn and Heaney, the two defining characteristics of a theory are that it must be applicable in a wide variety of circumstances (generalizability), and it must be testable.(109)

Theory is classified as 'explanatory' if it is used to describe factors that influence a behavior or situation, and as 'change' if it is used to guide the development of an intervention to a modifiable problem.(108) The relationship between 'explanatory' theory and 'change' theory often turns out to be cyclic due to the occurrence of the feedback process between the theories.

As illustrated in Figure 2.1, the underlying concern addressed by this dissertation was that the medical and economic resources used to treat asthma in the MHS were not resulting in optimum clinical and economic outcomes. A proposed explanatory theory for this problem was that unsatisfactory patient outcomes occurred because, until recently, there has been no formal process within the MHS to standardize asthma care. Outcomes management, and more specifically, the use of clinical practice guidelines

(CPGs), has recently been adopted by the MHS as a strategy to standardize asthma care.(14)

Figure 2.1 Relationship Between Explanatory Theory and Change Theory



(Adapted from Foundations of Applying Theory found at http://oc.nci.nih.gov/services/Theory_at_glance/PART_1.html)

2.4.2 Outcomes Management Theory

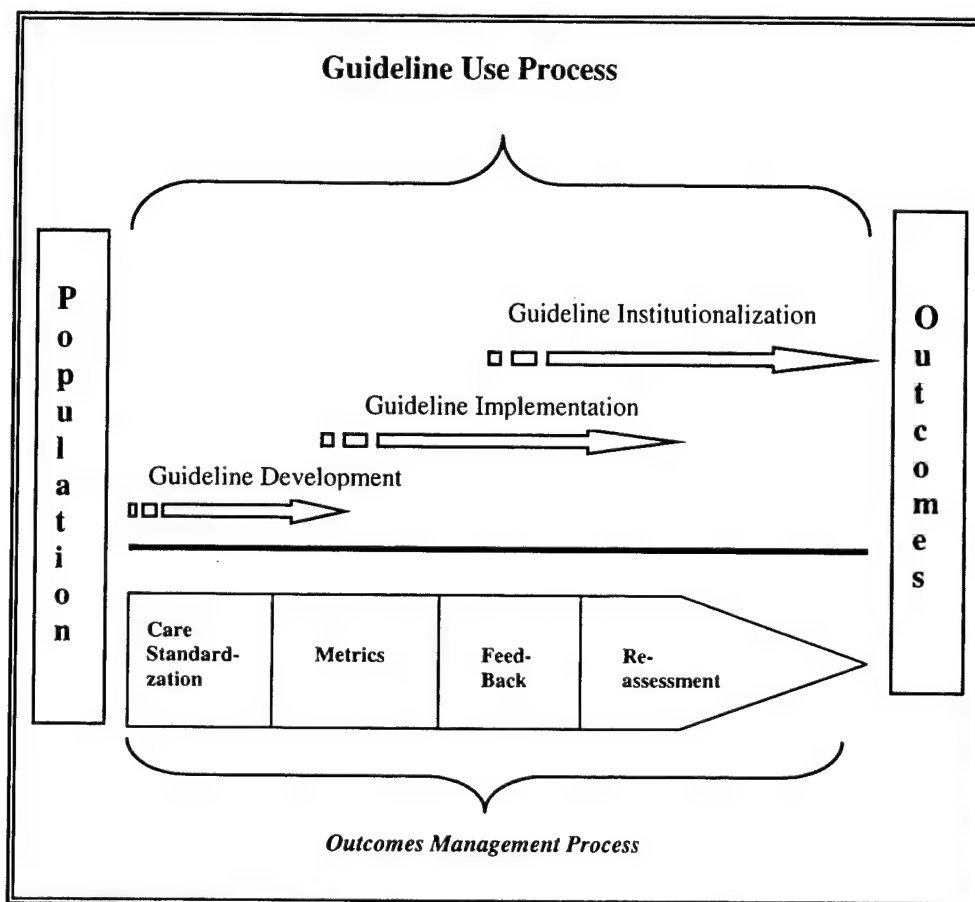
Outcomes management (OM) is a method of delivering care that relates characteristics of health services to patient outcomes.(110) When applied to a specific disease, OM is sometimes referred to as disease management.(111) Elwood describes OM as a

“technology of patient experience designed to help patients, payers and providers make rational medical care-related choices based on better insight into the effect of these choices on the patient’s life.”(110) Wojner describes OM as an integrated approach to health care based on a reimbursement scheme reflective of the natural course of disease, and treatment that is designed to address illness with maximum effectiveness and efficiency. He further states that OM reflects a patient-driven system of delivering health as opposed to physician or payer driven systems, which, in the past have been criticized respectively for their high cost or low quality.(112, 113) Four primary components of an OM system of providing health care, as described by Ellwood, are as follows:(110)

1. an emphasis on standards/guidelines for selecting appropriate interventions,
2. the measurement of patient functioning and well-being along with disease-specific clinical outcomes,
3. the pooling of clinical and outcome data, and
4. the analysis and dissemination of data to appropriate decision makers.

A parallel approach to the OM process, specific to guideline use, has been described by Nicholas.(14) This process, referred to as the guideline use process, consists of three stages: (1) development or adoption; (2) implementation; and (3) institutionalization. Figure 2.2 outlines the parallel nature and similarities between outcomes management and the guideline use process.

Figure 2.2: Application of the outcomes management process to the treatment of asthma within the military health system



Where: Population = Individuals treated by the military health system (MHS) with a diagnosis of asthma.

Outcomes = Asthma outcomes of individuals treated in the MHS.

One of the benefits of the OM process, or in this case the guideline use process, is that it provides useful information for testing theory. Data regarding outcomes of interest can be collected and analyzed at various times throughout a change process. Using Ellwood's OM process as a guide, this dissertation will test whether the efforts by the

MHS to standardize asthma care through the guideline use process, has resulted in improved outcomes for asthma patients. The first two steps of the process outlined above are ongoing; the Army Medical Department (AMEDD) has mandated the use of a formal guideline use process throughout its facilities, and data on patient outcomes has been recorded. The guideline use process has been adopted on a voluntary basis by the other military departments with varying degrees of use. In this dissertation, the second and third steps of Ellwood's OM process (pooling of data and analysis) are performed, and the formal guideline use process of the AMEDD evaluated.

2.4.3 Organizational Change Theory

2.4.3.1 Introduction

Critical to the success of using the three-stage CPG use process to improve asthma outcomes in the MHS, are strategies for disseminating CPG standards and for gaining their acceptance at all levels of the MHS organization. Developing a spirit of cooperation among the different MHS departments (Army, Navy, and Air Force) and ensuring that facilities in remote areas and environments are equally informed of the standards, are challenges unique to the MHS organization. Other challenges include overcoming barriers and resistance common to any organization whenever major changes are proposed.

The following section addresses the theoretical framework for creating effective organizational change. Kotter's eight steps of 'Leading Change' are discussed as are the

steps outlined by Langley in the “The Improvement Guide.”(114, 115) Two other approaches are discussed briefly. Within the context of each approach, reference is made to the corresponding stage of the guideline use process proposed by Nicholas.(14) Each theory, although varying in specific steps, is similar to each other in that it belongs to a broader type of theory known as stage theory. Change based on stage theory occurs in steps or stages. In its most abbreviated form, stage theory consists of four steps: problem definition (awareness), initiation of action (adoption), implementation, and institutionalization.(108)

2.4.3.2 ‘Leading Change’ (Kotter)

Kotter has developed an eight-step model for organizational change.(114) Although not specifically developed to facilitate guideline use, or for that matter adoption of other health care initiatives, the organizational change principles outlined in this model have application to both. The model is based on the fundamental insight that organizational change does not occur easily. Kotter suggests the following reasons why it is difficult to create organizational change: (1) inwardly focused cultures, (2) paralyzing bureaucracy, (3) parochial politics, (4) low level of trust, (5) lack of teamwork, (6) arrogant attitudes, (7) a lack of leadership in middle management, and (8) a general fear of the fear of the unknown.(114) The eight steps in Kotter’s model for organizational change are described below:

1. Establishing a Sense of Urgency – This step is especially important in the developmental phase of the guideline use process. Without a sense of urgency

few people are motivated to create change. The main barrier to establishing a sense of urgency is complacency. This can occur for any number of reasons and include: the lack of a highly visible crisis; too many visible resources; low overall performance standards; organizational structures that focus employees on narrow functional goals; internal measurement systems that focus on the wrong performance indexes; lack of feedback; low candor; a low-confrontation culture; or too much 'happy' talk from senior management.

2. Creating the Guiding Coalition – This step is also important to the development stage of the guideline use process. It involves putting together a group with enough power to lead the change. The four characteristics necessary for an effective guiding coalition are:
 - a. *Position power*: Having enough key players committed to the change so that those left out cannot easily block progress.
 - b. *Expertise*: Having various points of view, in terms of discipline, work experience, etc., adequately represented so that informed intelligent decisions will be made.
 - c. *Credibility*: Having individuals with good reputations (opinion leaders) so that recommendations will be taken seriously by others
 - d. *Leadership*: Having proven leaders in the coalition to drive the change process.

3. Developing a Vision and Strategy – This step is important to the development stage of guideline use in order to clarify or resolve issue regarding the direction of change. A clear vision, according to Kotter must be:
 - a. *Imaginable* – conveys a picture of what the future will look like;
 - b. *Desirable* – appeals to the long-term interests of all the stake-holders;
 - c. *Feasible* – comprises realistic, attainable goals;
 - d. *Flexible* – is general enough to allow individual initiatives and alternative responses in light of changing conditions; and
 - e. *Communicable* – easy to communicate.

4. Communicating the Change Vision – This is the process of transferring the change vision from theory to practice. Communicating the change vision is especially important during guideline implementation, however it is important to reinforce the vision at all stages of guideline use. Kotter offers the following suggestions for successfully communicating the change vision:
 - a. *Simplicity*: jargon/technical language should be minimal;
 - b. *Metaphor, analogy, and example*: pictures are worth a thousand words;
 - c. *Multiple forums*: multiple forms of spreading the vision are most effective;
 - d. *Repetition*: ideas are reinforced if heard multiple times;
 - e. *Leadership by example*: behavior consistent with the vision from key people is the strongest form of communication;

- f. *Explanation of seeming inconsistencies*: unaddressed inconsistencies can undermine the credibility of all communication; and
- g. *Give-and-take*: communication is more effective when it goes two ways.

5. Empowering Broad-Based Action – Kotter describes four broad barriers to successful change. These include: (a) formal structures that make it difficult to act; (b) actions by those in authority that discourage implementation; (c) a lack of needed skills undermines action; and (d) personnel and information systems that make it difficult to act. To overcome these barriers, Kotter makes the following suggestions:
 - a. Communicate a sensible vision to employees;
 - b. Make structures compatible with vision;
 - c. Provide adequate training;
 - d. Align information and personnel systems to vision; and
 - e. Confront authoritative personnel who undercut needed change.
6. Generating Short-Term Wins – This step of Kotter's organizational change model overlaps with both the implementation and institutionalization stages of guideline use. Short-term performance improvements can help the change process in a number of ways. These include the following:
 - a. Provide evidence (metrics) that sacrifices are worth it – wins greatly help justify the short-term costs involved;

- b. Help fine-tune vision and strategies – provide data to the guiding coalition on the viability of their ideas;
- c. Reward change agents for hard work – positive feedback builds morale and motivation;
- d. Undermine cynics and self-serving resisters – clear improvements make it difficult for change to be blocked;
- e. Keep bosses on board – provides evidence to those higher in the hierarchy that the change transformation is on track; and
- f. Build momentum – turns those who were neutral into supporters.

7. Consolidating Gains and Producing More Change - This step is important to the institutionalization stage of guideline use. Credibility established through small gains builds momentum. Momentum can manifest in a number of ways:

- a. More change – the guiding coalition uses credibility afforded by short-term wins to tackle additional and bigger change projects;
- b. More help – additional people are brought in, promoted, and developed to help with all the changes;
- c. Leadership from senior management – senior people focus on maintaining clarity of shared purpose for the overall effort/keep urgency levels up; and
- d. Project management and leadership from below –lower ranks in the hierarchy provide leadership and management of specific projects.

8. Anchoring – Anchoring occurs when new practices are assimilated into the old culture and become the standard of care. Kotter warns that anchoring a change into an existing culture is not easy and is only likely to occur if the new behavior can be linked to the production of a group benefit over an extended period of time. Kotter makes the following statements about anchoring change into a culture:
- a. Comes last, not first: most alterations in norms and shared values come at the end of the transformation process;
 - b. Depends on results: new approaches usually sink into a culture only after it's clear they work and are superior to old methods;
 - c. Requires a lot of talk: without verbal instruction and support, people are often reluctant to admit the validity of new practices;
 - d. May involve turnover: sometimes the only way to change a culture is to change key people; and
 - e. Makes decisions on succession crucial: if promotion processes are not changed to be compatible with the new practices, the old culture will reassert itself.

2.4.3.3 *'The Improvement Guide'* (Langley)

Another useful method for creating organizational change is the 'Model for Improvement' as described in *The Improvement Guide* by Langley and associates.(115)

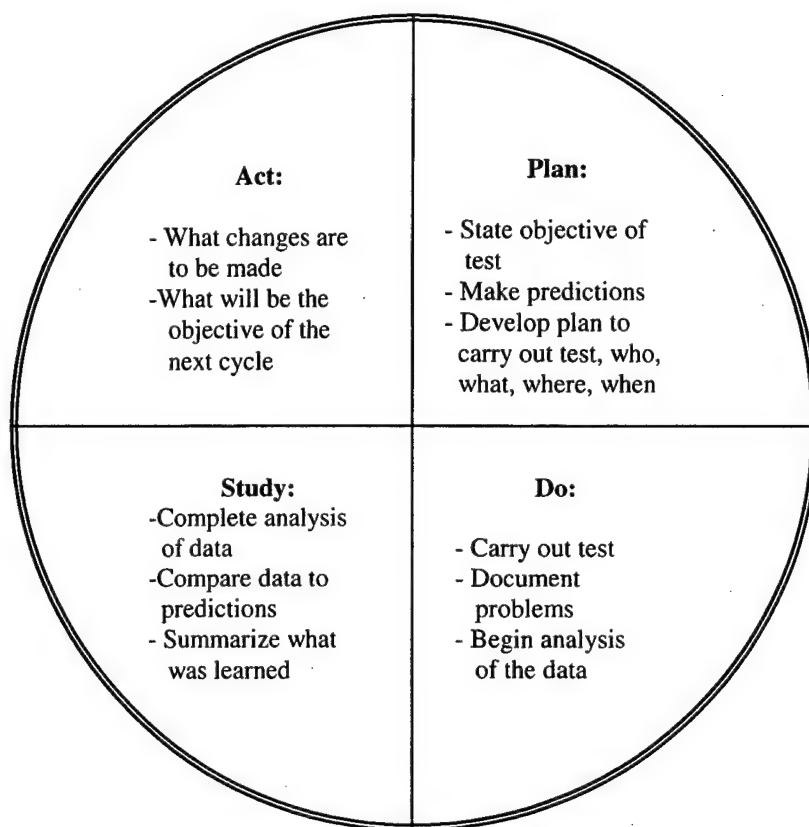
This approach to organizational change begins with three fundamental questions:

1. What are we trying to accomplish?
2. How will we know that a change is an improvement?
3. What changes can we make that will result in improvement?

The object of the first question is to guide and focus the effort by providing an aim to the improvement effort. The second question introduces the notion of criteria and measurement, and the third question provides a framework for what the authors call the “trial-and-learning” approach.

The Plan, Do, Study, Act (PDSA) cycle comprises the second part of the model. The two functions of the PDSA cycle are: (1) to test and evaluate the impact of a change, and (2) to learn about different alternatives.⁽¹¹⁵⁾ The cycle begins with a plan and ends with action based on the learning gained from the Plan, Do, and Study Phases of the cycle. The ‘Plan’ phase consists of planning the details of the test and making predictions about the outcomes. The ‘Do’ phase involves conducting the test and collecting data. The ‘Study’ phase compares predictions to the results of the test and the ‘Act’ phase involves taking action based on the new knowledge. Figure 2.3 summarizes the elements involved in each phase of the cycle when testing a change.

Figure 2.3 Elements of the PDSA Cycle

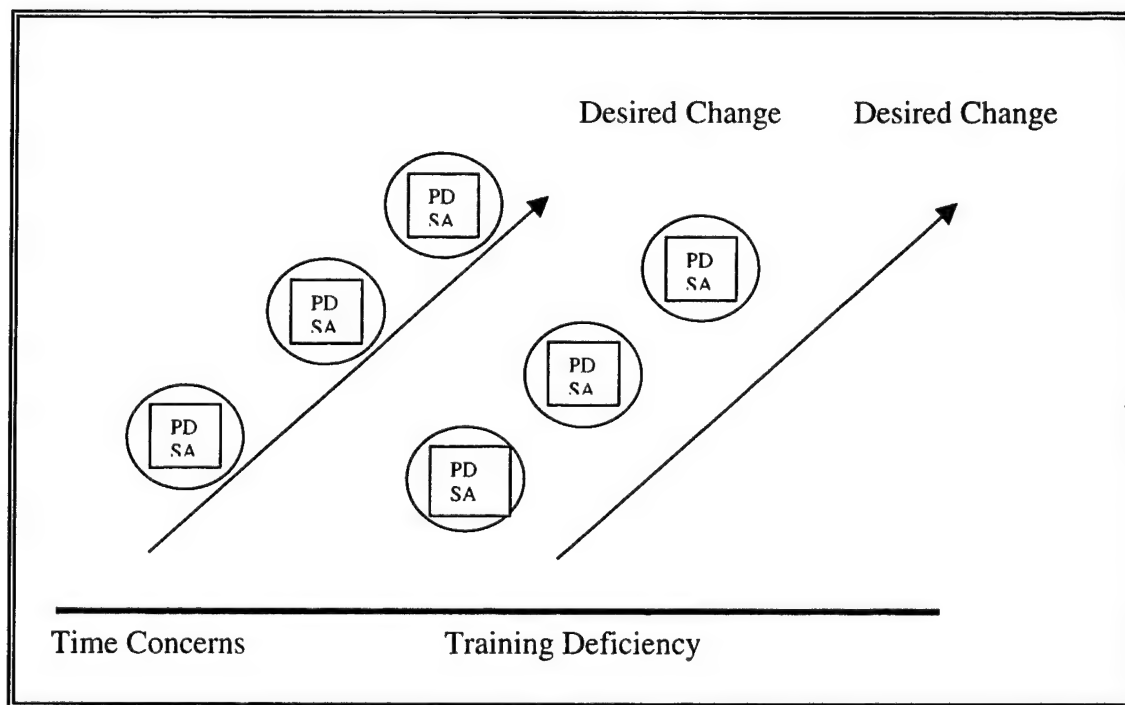


(Adapted from Langley et al. *The Improvement Guide: A Practical Approach to Enhancing Organizational Performance*. 1966, JOSSEY-BASS, San Francisco)

The combination of the three 'fundamental' questions and the PDSA cycle is referred to as 'The Model for Improvement.' According to Langley, the model can be used in quality improvement efforts to: (1) build knowledge; (2) test a change; and (3) implement a change. An advantage of the 'Model for Improvement' is that the PDSA cycle can be used sequentially to address numerous issues or barriers simultaneously as illustrated in Figure 2.4. Each of the arrows represents an action for improvement that moves through successive cycles, until the desired change is achieved. One potential

limitation of using this technique is that it may not always be obvious which cycle produced the desired change. To address this issue, Langley discusses a type of 'sensitivity analysis' in which changes are turned 'on' and 'off', one at time, to evaluate changes in performance.(115) Langley also raises the possibility that no single change or sequence of changes is responsible for the overall improvement, but rather the newly designed system as a whole is responsible for the increased performance.

Figure 2.4: Using Sequences of PDSA Cycles to Simultaneously Solve Barriers to Guideline Implementation



(Adapted from Langley et al. The Improvement Guide: A Practical Approach to Enhancing Organizational Performance. 1966, JOSSEY-BASS, San Francisco)

In terms of fitting Langley's 'Model for Improvement' to the guideline use process, the guideline development/adoption phase of the process could be addressed using the three fundamental questions of Langley's model, with some overlap to 'Plan' element of the PDSA cycle. The implementation and institutionalization phases would be addressed in the context of the PDSA cycle.

2.4.3.4 Other Change Models

Other approaches and models for organizational change have been described in the literature. One, the 'Precede-Proceed' model designed by Green and Kreuter is based on the principle that most enduring changes are voluntary in nature.(116) This principle is reflected in a nine-phase systematic planning process which seeks to empower individuals with understanding, motivation, and skills. Although designed specifically for use in health education and health promotion programs, certain aspects of this theory could be applicable to guideline use. The five-step 'Diffusion-Model' also has merit in developing a change strategy. Starting from a base of knowledge, the change process progresses through steps of persuasion, decision, implementation, and confirmation.(108) Another change theory is 'The Innovation Process in an Organization.' This is a two-phase model that is completed over five steps. The first phase, initiation, consists of defining the problem (agenda setting) and then fitting the problem with an innovation (matching). This is followed by the implementation phase which consists of modifying the innovation to fit the organization needs (redefining), clarifying the relationship

between the innovation and problem (clarifying), and finally, ensuring the innovation becomes an ongoing element in the organizations activities (making routine).(108)

Wensing and associates argue that a combination of theories is sometimes necessary to create organizational change. This makes intuitive sense, especially with a stepwise approach to change, since as Chalmers points out it would be expected that each step in the process of change would be associated with a different set of barriers or problems.(117)

2.4.3.5 Guideline Applications

The previous section discussed general approaches to creating organizational change. The following section will discuss issues specific to organizational change caused by guideline use. Issues related to guideline development and/or adoption will be discussed first, followed by guideline implementation, and finally guideline institutionalization.

2.4.3.5.1 Guideline Development/Adoption

The decision to use clinical practice guidelines is generally made by the leadership of a health care organization. Whether guidelines are built from scratch, or adopted from an organization such as the Agency for Health Care Policy and Research (AHCPR), the process can be complex and time consuming. According to Woolf, guideline development is a seven-step process which is best accomplished through a multidisciplinary panel that includes physicians and usually, other health professionals

(eg., nurses, pharmacists), methodologists (eg., epidemiologists, statisticians), health economists, and members of other disciplines. Additionally, some panels may include patients and consumer representatives. Although the first three steps of the development process usually occur in chronological order, some overlap can occur between the last four steps. Each of these steps is discussed below.

Step 1: Definition of Topic and Process - The first step in guideline development, according to both Woolf and Thomson, is the selection and definition of an appropriate subject or topic.(118, 119) Topics of practice guidelines are generally either *conditions*, such as asthma, or *procedures*. They can focus on prevention, diagnosis, treatment, or rehabilitation. Although the general outlines of the topic are usually known ahead of time, this first step requires the development of more precise definitions. Thomson strongly discourages choosing a guideline topic simply because of a desire for guideline use in that area – instead he suggests the following criteria be used to guide the selection process:(118)

- Is the topic high volume, high risk, high cost?
- Are there large or unexplained variations in practice?
- Is the topic important in terms of the process and outcome of patient care?
- Is there potential for improvement?
- Is the investment of time and money likely to be repaid?
- Is the topic likely to hold the interest of team members?
- Is consensus likely?

- Will change benefit patients?
- Can change be implemented?

In addition, Baker and Feder argue that an appropriate topic needs to be sufficiently complex to require more than one recommendation. If not, they argue that therapeutic action is better accomplished through a single recommendation derived from quality research without the rigors of developing a guideline.(120) Defining the topic includes specification of the target condition, the type of patients and clinical presentations for which the guidelines are intended, and the interventions to be considered.(79)

Step 2: Systematic Review –Woolf describes the systematic review as a three-stage process. First is the retrieval of evidence. This involves the collection of admissible evidence from relevant articles, books, and reports.(121, 122) Evaluation of individual studies is the next step. This involves assessment of the quality of the evidence, based on the study design features. Such factors as selection bias, confounding variables, and data analysis should be considered.(123, 124) Lastly, a synthesis of the evidence needs to occur. This is the combining of evidence from multiple studies to reach conclusions about the overall weight of the evidence on a particular study.(119)

Step 3: Consideration of expert opinion - It is sometimes necessary to rely on clinical experience and expert opinion when high-quality evidence is lacking on a specific subject. The alternative to this step is to simply state there is insufficient evidence to

make a recommendation or to qualify a judgment as being opinion based. The opinions of panel members can be assessed through informal techniques such as open discussion or simple voting, or through more formal methods such as the Delphi method.(125)

However the process is accomplished, the opinions and rationale of those contributing to the discussion should be documented so that readers are aware of which sections of the recommendations are based on opinion.

Step 4: Public Policy Considerations – This step of guideline development balances decisions and recommendations made through systematic review and expert opinion with other influences that shape health care policy. For example, resource and feasibility issues may force considerations of cost effectiveness, availability of technology and personnel trade-offs with other medical strategies, and patient access to services. According to Cook, some of the public policy concerns associated with guidelines have not been evaluated sufficiently. In a systematic review of guideline implementation, she reported 'process of care' improvements in 55 of 59, and patient outcome improvements in 12 of 17 studies; however no such summaries have been conducted to evaluate costs.(126)

Other public policy considerations, such as ethical considerations and the acceptability of interventions to patients and society, may influence decisions. Berger and Rosner address a number of the ethical considerations; the primary concern being the motivation for which the guidelines are being developed. They argue that practice guidelines are not

simply assistive tools for clinicians but are a highly diverse collection of instruments used as policy and policing devices and that these applications reflect values that are not necessarily patient centered. They also recommend that although guidelines can be an indispensable clinical tool, inappropriate nonclinical applications and unwarranted enforcements are problematic. Enforcement practices for nonclinical applications of guidelines must be scrutinized for consistency with notions of professionalism, informed patient consent, and patient benefit.(72)

Other public policy issues associated with guideline use include potential effects on insurance and malpractice. Since these issues are often outside the realm of expertise of medical practitioners and researchers, it is sometimes necessary to seek input from experts in other fields such as health economists, patient representatives, attorneys, government representatives or manufacturers, on the guideline panel. According to Woolf, it is at this stage of guideline development that panel members are most likely to struggle with conflicts of interests.(70)

Step 5 – Development of Recommendations – Clear documentation of the supporting evidence used to make specific recommendations should be established in this step.(126) In an evaluation of guideline methodology, Shaneyfelt reported that only 7.5 percent of 279 guidelines described the methods used to combine evidence and expert opinion.(127) Woolf suggests the use of a scoring system, based upon explicit criteria, be used to summarize the strength of evidence associated with a recommendation.(119) For

example, the U.S. Preventive Services Task Force uses a five-tier grading system to summarize preventive service recommendations. Studies with the strongest designs and highest level of supporting evidence are scored highest with a designation of 'A.' As the strength of the study design and/or supporting evidence decreases, so does the alphabetic designation. The letter 'E' is the lowest score possible and designates a recommendation based upon an observation design with no supporting evidence.(128) Another widely accepted system of classifying the quality of medical literature is presented by Guyatt et al. This is a six-tiered system, again based on the level of supporting evidence and study design.(129)

Step 6: Document Preparation – Most evidence-based guidelines have several versions. A full report is usually prepared for those desiring to examine all of the evidence, while a shorter version is prepared for journal publication and clinician use. Often an even more abbreviated form will be made available for dissemination to the lay public.

Step 7: External Review – An important step in guideline development is the external review. At this stage, guideline recommendations are reviewed by content experts to ensure scientific and clinical validity. Additionally, they are reviewed for structure compatibility by organizations and agencies with a stake in their use. Presenting draft versions at professional meetings is one method of obtaining important feedback before the completion of the final product.(130) Another method to get feedback is through pretesting. A small sample of practitioners is asked to use the guideline for a brief period

of time, following which suggestions are collected and used to make improvements in the guideline.

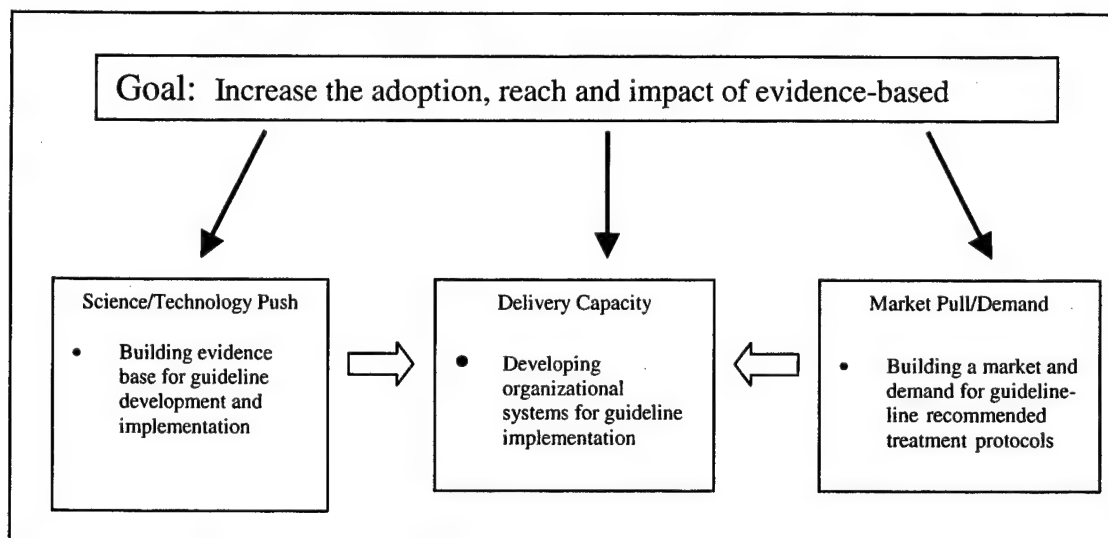
2.4.3.5.2 Guideline Implementation

The ultimate goal of implementation is to fully incorporate guideline recommendations in the clinical practices of the health care organization. Guideline development does not ensure implementation of forthcoming recommendations, nor does it guarantee improved outcomes.(131) In fact, as Smith states, efforts to implement guidelines often meet with failure.(77) This is frustrating, not only to clinicians interested in improving their own practice but to others, such as researchers, policy makers, and administrators, who have a stake in the use of guidelines.(132)

Curry argues that to effectively implement guidelines, the recommendations need to be accepted and supported at three levels - patient, provider, and organizational.(75)

Anderson and co-workers describe the interaction or 'synergy' between these three levels in what they call the "push-pull-capacity" model.(133) According to the model (Figure 2.5), the 'Push' occurs when science and technology generate enough evidence for credible guidelines to be developed. The 'Pull', or demand, is created from guideline users. This includes patients who desire state-of-the-art treatments, providers wishing to engage in best practices, and organizations that are trying to enhance efficiency, control costs, or improve health outcomes. Lastly, the 'Delivery Capacity' refers to the development of systems within the organization for guideline implementation.

Figure 2.5 Synergistic Model to Enhance Guideline Implementation



Although considerable progress has been made to establish the evidence or 'Push' element of the model for certain disease states, establishing success in the other two elements of the model has been more difficult. According to Smith, there is no 'magic bullet' for developing a *Market Pull* or *Demand* for guidelines, especially in the provider market.⁽⁷⁷⁾ Adherence to guideline recommendations generally requires a change in a provider's current method of delivering care. A number of reasons why modifying physician behavior may be difficult are suggested. The first has to do with the physicians' 'professionalism,' namely their prior education, scientific bent, and code of ethics. Smith argues that because of the rigors of medical school, including influences by opinion leaders, mentors, and peers; many of the normative behaviors physicians carry into their medical practice have already been established by the time they finish their formal medical training. Furthermore, Smith suggests that because of the repetitive

nature of much of the training, the resulting normative behavior is more closely related to ingrained reflexes or habits, as opposed to behaviors based on cognition or reasoning, which generally are easier to change.(77) Another factor that contributes to the complexity of physician behavior includes what Smith calls the physician's 'humanity,' a trait which can vary considerably from one physician to another. This includes the personal needs, desires, social system, and environment within which the physician functions. Lastly, the multiple interests, pressures, and interactions with the patient, society and, increasingly, the payer also help to meld behavior patterns of physicians. Grol suggests that no one theory is adequate to cover all of the multiple motivations and factors associated with physician behavior.(134) Instead, he and others argue that several theories, often applied in a stepwise manner, may be needed to realize a change in physician behavior.(134, 135, 136, 137) These theories are summarized in Table 2.6. by whether they focus on internal processes or on external processes.(134)

Table 2.6 – Theories and Approaches to Physician Behavior Change

Approach	Theories	Focus	Intervention Strategy
<i>Focus on internal processes</i>			
Educational	Adult learning theories	Intrinsic motivation of professionals.	Bottom up, local consensus development. Small group interactive learning. Problem-based learning.
Epidemiologic	Cognitive theories	Rational information seeking and decision making .	Evidence-based guideline development. Disseminating research findings through courses, mailing, journals.
Marketing	Health promotion, innovation and social marketing theories	Attractive product adapted to needs of target audience.	Needs assessment, adapting change proposal to local need Stepwise approach. Various channels for dissemination
<i>Focus on external influences</i>			
Behavioral	Learning theory	Controlling performance by external stimuli.	Audit and feedback. Reminder systems, monitoring, economic incentives, sanctions.
Social interaction	Social learning and innovation. Theories: social influence and power theories.	Social influence of significant peers/ role models.	Peer review in local networks. Outreach visits (academic detailing). Individual instruction. Opinion leaders. Influencing people in social networks. Patient mediated interventions.

Table 2.6: Continued

Theories and Approaches to Physician Behavior Change

Approach	Theories	Focus	Intervention Strategy
<i>Focus on external influences</i>			
Organizational	Management theories. System theories.	Creating structural and organizational conditions to improve care.	Reengineering care process. Total quality management/ continuous quality improvement approaches. Team building. Enhancing leadership. Changing structure, tasks.
Coercive	Economic, power, and learning theories.	Control and pressure, external motivation.	Regulation, laws, budgeting, contracting. Licensing, accreditation complaints/legal procedures.

Adapted from: Grol R. Personal paper. Beliefs and evidence in changing clinical practice. BMJ 1997;315:418-21

The literature cites numerous examples of barriers that impede the acceptance of guidelines by physicians or other providers. Cranney classifies barriers into three categories: structural (workload, lack of ready access to protocols, inadequate computerization); attitudinal (ageist attitudes, a reluctance to adhere to protocols where they exist, and other practice priorities), and educational (methods of education).

Another classification system places barriers into four broad, and sometimes overlapping categories: (1) guideline development/methodology issues; (2) preference and autonomy issues; (3) clinical issues; and (4) bureaucratic/structure issues.

Lack of confidence in the methods used to develop guidelines has been a major barrier to their use. Shanneyfelt and associates, in a review of 279 guidelines, reported that only 51 percent adhered to methodological standards on guideline development and only 40 percent specified the outcomes of interest. Other issues of concern they reported included poor descriptions of the patient population and a failure to describe audience for which the guideline was intended. They also reported that few guidelines specified the methods used to identify scientific evidence (16.8%), the methods used for combining evidence (7.5%) or the time period (14.3%) over which the evidence was collected.

Mention of projected effects on health care costs occurred in only 41.6% of the reviewed guidelines and only 21.5% discussed the role of patient preferences in choosing among available options.⁽¹²⁷⁾ In another study, Bero and associates reported that common methodologic problems included the failure to report selection criteria for studies, the failure to avoid bias in the selection of studies, the failure to adequately report criteria

used to assess validity, and the failure to apply criteria to assess the validity of the selected studies.(15)

Another methodological concern raised by Graham and coworkers was the assessment of external validity, especially with guidelines developed for use in chronic diseases. They argue that a number of biases, including patient, physician, organizational, and system factors, affect the generalizability or applicability of recommendations to primary care clinical practice. Further, they state that these factors can undermine measurement, and ultimately evaluation of, physician adherence to clinical review criteria.(138)

A concern about the ability to generalize guideline recommendations has been stated as another reason why physicians are reluctant to use them. Halpern argues that although practice guidelines may define a benefit for the average patient, it doesn't necessarily reflect what the needs of a specific patient are.(139) This argument was also used by Asch and Hershey in describing how the risks associated with a specific guideline recommendation may vary among different individuals. They argue that the more individual patients vary in a response to a treatment, the less a population-based analysis (guideline) should be trusted for individual decisions.(140)

Reluctance to use guidelines can also occur for reasons personal to the provider. The need for some measure of physician autonomy and clinical discretion form the basis for a good part of physician objection to coercive enforcement of guidelines. Long-held personal values and biases as well as litigation concerns can drive physicians either

toward or against the use of guidelines.(72) A 1994 survey of American College of Physician members indicated that 43 percent of those surveyed believed that guidelines would increase health care costs, 68 percent believed that guidelines would be used to discipline physicians, and 34 percent believed they would make medical practice less satisfying.(141) Woolf states that physician reluctance to embrace guideline use may also be associated with fears of the misapplication of practice guidelines as punitive devices by government, payers, courts, licensing and certification boards, or administrators.(79) Along these same lines, Berger expresses a concern over the potential to use guidelines for evaluating the clinical competence of physicians or to question their use of medical resources.(72) Additionally, physicians may see guidelines as an avenue for other health care professions to assert themselves into the traditionally physician held role as 'providers.' Although not universal, some physicians have expressed mixed emotions with the expanding 'provider' role of other health care professions. In a recent editorial, this frustration was apparent in the words of one physician as he expressed his resentment with the term 'provider' being applied to physicians. He stated that being called a 'provider' not only diminished him as a professional but lumped he and his physician colleagues in the same category as other less qualified professionals aspiring to do the same work.(142) There is little doubt that guideline use has increased the role of ancillary health care professionals such as physician assistants, nurse practitioners, and clinical pharmacists, in the delivery of health care.(143, 144)

Some providers have cited clinical irrelevancy or inconsistencies between guidelines as barriers. Berger points out that especially in the managed care environment, physicians may be involved with numerous health care plans that either overlap or use entirely different guideline requirements. He also points out that oversight organizations, in the areas of quality and utilization, are likely to apply the same guideline differently. Both of these situations have the potential to give physicians the perception that guidelines are applied inconsistently.(72) Berger also points out that the management of some clinical entities is not amenable to strict guideline application. In these cases, rigid guideline enforcement may preclude unapproved but beneficial applications of existing treatments.(72)

The bureaucratic or structural environment of an organization has much to do with a providers perception of the guideline process. According to Sonnad, without an effective interface between the developers and users of guidelines, it is highly probable that a high degree of uncertainty and controversy will occur during the adoption and implementation process.(145) Additionally, guideline implementation can be costly. Organizations unwilling to provide additional technical and personnel resources in the guideline process could likely encounter resistance by providers based on the perception that an already bulging workload for themselves and their staff is to be expanded even further.(104) Suggestions by Heffner for working through some of these barriers include the use of computer systems, academic detailing, recruitment of local medical opinion leaders, performance measures, educational outreach, and continuing education.(69) Table 2.7

summarizes these barriers and suggests which types of theories might be useful in addressing them.

The other *Market Pull* or *Demand* that is influential in guideline implementation is the intervention of organizations. According to Curry, three major organizational structures contribute to the pull-push-capacity model. These include national organizations, such as professional associations; federal agencies devoted to health care, and regulatory or accreditation bodies; health-care organizations, which can be local, regional, or nationwide; and purchaser groups.(75)

A review by Shaneyfelt and associates suggested that guidelines are produced by a wide variety of health care organizations. Of the 279 guidelines included in the review, 45 percent were produced by subspecialty medical societies, 33 percent by general medical societies, 16 percent by government agencies, and six percent by miscellaneous groups that could not be classified.(127) Regardless of which level of organization guidelines are produced, Shaneyfelt recommends adherence to the following characteristics as key to provider acceptance: evidence-based (synthesis of evidence from large-scale randomized trials, observational studies, and expert opinion); simplicity and clarity; congruence with prevailing practice; and, goals that are explicit and measurable.

Techniques used by some organizations to impart credibility to guidelines include giving them public endorsement and developing ways to change practice norms to align with the

new guidelines.(75) As Curry notes, the use of guidelines is also promoted within some organizations as a method of meeting the requirements of agencies that provide accreditation and “report cards” for health-care organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) or the National Committee on Quality Assurance (NCQA). Accrediting organizations often look to guidelines for determining which clinical outcomes to include in benchmarks for assessing quality of care. Likewise, regulatory and quality-rating requirements strongly influence the clinical priorities of health care organizations. It is not uncommon for health-care organizations to accelerate the adoption and compliance of guidelines in response to requirements of accrediting organizations.(75)

Table 2.7: Barriers to Guideline Implementation

	Barrier	Citation	Potential theory response	Affected Market Group
Guideline design	Standardization issues including nomenclature, development, use of scientific data, purpose, mechanism for updating	Berger & Rosner(72)	Cognitive theories. Adult learning theories (internal). Management and system theories (external).	Providers
	Use of unsound methodology	Shaneyfelt(127)	Cognitive theories. Adult learning theories (Internal).	Providers
	Validity issues (Internal and External)	Berger & Rosner(72) Cook et al.(126) Graham et al.(138) Bero et al.(15, 138)	Cognitive theories (Internal).	Providers
	Lack of supporting evidence	Berger & Rosner(72) Shanyfelt(127) Cook et al.(126)	Cognitive theories (internal).	Providers
	Complexity of guidelines	Berger & Rosner(72)	Cognitive, and adult learning theories (internal). Organizational (external).	Providers
Personal/ autonomy	Defacto standards through enforcement	Berger & Rosner(72)	Power and learning theories. Management and system theories. (external).	Providers
	Lack of 'front-line' practitioner involvement in guideline development	Woolf(70)	Adult learning theories. Cognitive theories (internal). Management and system theories. Economic, power, and learning theories (external).	Providers
	Malpractice/discipline concerns	Woolf(70) Berger & Rosner(72)	Adult learning theories (internal). Economic, power, and learning theories (external).	Providers Organizations

	Barrier	Citation	Potential theory response	Affected Market Group
<i>Personal/ autonomy</i>	Ethical concerns	Berger & Rosner(72) Cook et al. (126) Gevers(103)	Cognitive theories. Adult learning theories (internal). Social learning, influence, and power theories. (external)	Providers Organizations
	Time intensive to follow guidelines/Workload	Curry(75) Cranney et al.(146) Cabana et al.(147)	Adult learning theories (internal). Economic, power, and learning theories. Management and system theories.	Providers Organizations
	Ageist attitudes	Cranney(146)	Adult learning theories (internal). Economic, power, and learning theories. Management and system theories.	Providers, Organi- zations
<i>Clinical</i>	Conflict between guidelines	Berger & Rosner(72)	Cognitive theories. Adult learning theories (internal). Social learning and innovation theories. Management and system theories (external).	Providers Organizations
	Clinical irrelevancy	Berger & Rosner(72)	Cognitive theories. Adult learning theories (internal). Social learning and innovation theories. Management and system theories (external).	Providers Organizations
<i>Bureau- cratic</i>	Organizational problems	Berger & Rosner(72)	Management and system theories (external).	Organizations Providers
	Implementation concerns	Berger & Rosner(72)	Health promotion, innovation and social marketing theories (internal). Learning, management and system theories. Economic, power, and learning theories. Social learning and innovation theories (external).	Providers Organizations
Table 2.7: Continued				

	<i>Barrier</i>	<i>Citation</i>	<i>Potential theory response</i>	<i>Affected Market Group</i>
<i>Bureaucratic</i>	Cost concerns	Cook et al. (126)	Cognitive theories. Economic theories.	Organizations Providers
	Inadequate computerization	Cranney.(146)	Management and system theories. (external).	Providers, Organizations
	Concerns regarding cost-effectiveness at patient level versus population level	Cook et al. (126)	Cognitive theories. Economic theories.	Organizations Providers
	Poor cost summarization in majority of guidelines	Cook et al. (126)	Cognitive theories. Economic theories.	Organizations Providers

Table 2.7: Continued

Guideline strategies utilized by the insurance industry can also impact the *Market Pull* or *Demand* from an organizational perspective. Health-care organizations and insurers can encourage guideline implementation through their benefit structures, the administrative and technological resources they make available to practices, and the accountabilities they establish for physicians. Additionally, the allocation of resources for guideline training can be helpful in generating acceptance of guidelines. Several studies suggest that organizations can benefit greatly through the use of the 'academic detailing model' to conduct their training. This model utilizes trainers who are local experts, opinion leaders, or guideline champions to lead the change efforts.(148, 149) Another tactic that is sometimes used by insurance/health-care organizations to promote the use of guidelines is to link guideline-related outcomes to performance accountabilities for physician evaluation and compensation. Reporting of these outcomes can also tie in with what ever quality assurance strategy that is being used by the organization.(150)

Strategies of purchasers of health care can also influence the organizational *Market Pull* element of the 'Push-Pull-Capacity' model. Several studies suggest that over the past decade employers have become the largest purchasers of health care in the United States.(97, 98) Purchasers have responded to the rising costs of health care in various ways. These include limiting health care choices to certain HMOs, requiring employees to share health-care premium costs, direct contracting between employer coalitions and health-care provider systems, and implementing self-insurance plans.(97, 98) In at least

one study, guidelines were found to be an important negotiating tool for purchasers in their negotiations with health-care organizations over benefit packages.(96)

The last element of Anderson's 'Push-Pull-Capacity' model is the *delivery capacity* of the organization. This is the combination of techniques and strategies used within an individual organization, to foster the use of guidelines. To facilitate *delivery capacity*, Curry suggests the follows actions:(75)

- Provide benefit coverage (for patients) and/or reimbursement (for physicians) for guideline based treatment protocols.
- Implement clinical information systems that allow for the following: (1) population-based tracking of patient populations; (2) monitoring of outcomes to assess progress in guideline implementation; and (3) benchmarking feedback to physicians.

In addition to the 'Push-Pull-Capacity' model developed by Anderson, a number of other theories for guideline development have been published. As previously discussed, Table 2.6 summarizes some of the more widely cited theories and common elements between them.

2.4.4.3.5.3 Guideline Institutionalization

Institutionalization occurs when a new methodology becomes part of the standard of care. This often requires the combination of a number of factors. The support and active involvement of the health care organization leadership is of paramount importance. In addition, Nicholas stresses two other keys to success. One is to build local ownership or buy-in of the guideline process and the other is to provide clinical and administrative system support.(14)

A strategy consisting of six separate, but sometimes overlapping, steps is suggested for building local ownership:

- Use opinion leaders – communication with appropriate staff regarding guideline implementation should be spearheaded by a respected opinion leader – sometimes referred to as the guideline champion
- Educate staff – becoming familiar with the contents of a guideline is the first step toward accepting it. Educational seminars, small group discussions, or using guideline logic to simulate cases are effective means of providing education.
- Focus on local implications – demonstrate to the staff how the guideline fits into the clinical context of the health care facility. With cooperation of the guideline stakeholders, identify what areas of clinical care will be most positively or negatively affected by the guideline.

- Include all levels of staff – education and training should include all levels of staff involved in implementation. This should include primary care physicians, nurses, specialists, nurse practitioners, pharmacists, physical therapists, nutritionists, support staff, etc.
- Focus on improving patient outcomes – how guidelines will be used to improve the quality of patient care should be publicized
- Use data when possible – the use of data to support guideline can build a stronger case for local relevance

Goldberg and associates suggest several additional techniques to build local ownership.(151) The first, academic detailing, was modeled after methods used by pharmaceutical sales representatives.(152) This technique involves the training of physicians, pharmacists, or other health care professionals to offer providers brief, one-on-one education and feedback sessions. Another, more complex technique, is continuous quality improvement (CQI). This requires the entire organization to commit to reducing unwanted practice variation at all levels, with multidisciplinary teams being empowered to make changes in sub optimal processes and to monitor whether or not the stated goals are achieved.(153)

In order for institutionalization to occur, guidelines need to have more than just the enthusiasm and commitment of those who support them. Nicholas argues that to realize lasting improvements in clinical practices and patient outcomes, a wide array of staff

resources and administrative and clinical systems need to be coordinated. This can be accomplished in several ways:

- Emphasize systems over individual behavior – it should be stressed to providers and clinic staff that guideline implementation is concerned more with modifying and/or creating systems to support clinical behaviors than about policing the actions of individual practitioners.
- Understand current processes – Flow charts are a useful tool to gain a better understanding of exactly what the current processes are. Map out all clinical and administrative processes that are relevant to guideline implementation.
- Identify needed changes – tap the expertise of the health care facility to identify the system changes that need to be made to accommodate the guidelines. If there is insufficient information to identify needed changes, work with the staff to gather the needed information.
- Involve a variety of staff members in changing systems – Nicholas argues that better results will be achieved, and support of the program will be underpinned, if all levels of support staff are used in system changes.
- Use process data to measure change – track progress of the new or modified systems by measuring changes in the care processes. Respond to unexpected results quickly.

2.5 Guideline Use in Asthma

In the previous sections, both general approaches to organizational change and issues specific to change as a result of guideline implementation were discussed. This section will review the application of guidelines to the treatment of asthma. The discussion will begin with an overview of the National Asthma Education and Prevention Program (NAEPP) and its guideline development process. The components of the NAEPP guidelines will then be described. Following this a description of asthma guideline use in the DoD.

2.5.1 National Asthma Education and Prevention Program (NAEPP)

The primary guideline initiative for asthma in the United States has come through the work of the National Asthma Education and Prevention Program (NAEPP). An understanding of this initiative is important as it forms the foundation for the majority of asthma guidelines in use in the United States today. The NAEPP, initiated in 1989 to address the growing problem of asthma in the United States, is administered and coordinated by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). The goals of the NAEPP are stated to be:(154)

- Raise awareness of patients, health professionals, and the public that asthma is a serious chronic disease.
- Ensure the recognition of the symptoms of asthma by patients, families, and the public and the appropriate diagnosis by health professionals.

- Ensure effective control of asthma by encouraging a partnership among patients, physicians, and other health professionals through modern treatment and education programs.

2.5.2 NAEPP Asthma Guideline Development

As discussed in section 2.3.6.2, guideline development can be described as a seven-step process. The summary of this process as applied to the NAEPP asthma guideline development is described below:

Definition of Topic and Process

To help meet their asthma goals, the NHLBI convened panels of experts twice to prepare objectives and then guidelines for the diagnosis and management of asthma. The first Expert Panel Report was released in 1991. The second, an updated version addressing improvements made in the understanding of the disease process and new approaches to therapy, was released in 1997. The definition of asthma and the need to develop guidelines are addressed in the introduction and first chapter of the 1997 report. A background providing documentation for both the importance and appropriateness of asthma as a guideline topic are also found in this section of the guidelines. Some of the issues addressed in the background section include the increasing prevalence of asthma, the associated morbidity, and mortality, and the costs – both direct and indirect – of providing treating those with asthma. Development of objectives to meet the overall goals of the NAEPP guidelines could also be considered part of this first step. Two sets

of objectives were developed to operationalize the NAEPP goals - one for patients and the public, and the other for health professionals:(154) The patient/public objectives emphasized methods for: (1) increasing public awareness of asthma as a significant public health problem; (2) detecting signs and symptoms of asthma, and (3) improving knowledge regarding treatment and control of asthma. The objectives for health professionals addressed the need to improve diagnostic and monitoring skills, and methods to promote and encourage the concept of active patient participation with the provider in asthma management. Both sets of objectives (patient/public and health professional) relied heavily upon the use educational techniques for their success.

Systematic Review

The recommendations of the 1997 Expert Panel Report (EPR-2) were based on the culmination of more than four years of preparatory analysis, meetings, writings, and review cycles. The EPR-2 built upon the 1991 Expert Panel Report (EPR-1) and added recommendations for clinicians and patients about such important issues as the appropriate medications for controlling asthma.(154) The final recommendations of the EPR-2 were synthesized from the evidence of over 6000 scientific articles identified through a series of MEDLINE database searches.(53)

Consideration of Expert Opinion

The expert panel for the EPR-2 was a multidisciplinary group of clinicians and scientists who had asthma management expertise and who were representative of clinicians who

cared for patients with asthma. It included professionals from general medicine, family practice, pediatrics, allergy, pulmonary medicine, nursing, pharmacy, and health education. The panel developed its recommendations using a modified Delphi approach with careful consideration for the nature and quality of the study designs.(155)

Public Policy Considerations

Among the public policy considerations that guidelines should address - those of cost, ethics, and malpractice issues are primary. A main criticism of the EPR-1 guidelines came from emergency room physicians. They questioned the makeup of the Expert Panel (mostly allergists, immunologists, and pulmonologists), and warned of the implications of practicing "cookbook" medicine, since the 'effectiveness' of these guidelines had not been studied in the Emergency Department.(156) To address the ethical and malpractice implications of these concerns, efforts were made in the selection of clinicians and scientists, to ensure a multidisciplinary makeup of the EPR-2 panel. Additionally in the EPR-2, branching guidelines in the form of algorithms or flowcharts were used allowing for greater treatment flexibility. This helped remove some of the criticisms that were associated with the deterministic guidelines found in the EPR-1.(3)

The impact of guidelines on the cost of asthma is discussed only briefly in the report. The report states that implementation of EPR-2 recommendations is likely to raise some costs of asthma care by increasing the number of primary care visits for asthma and the use of asthma medications, environmental control products and services, and equipment.

However, EPR-2 goes on to argue that the total costs associated with asthma will be decreased by guideline use. This is a result of a decrease in hospitalizations, emergency department visits, deaths and lost work/school days associated with asthma due to better diagnosis and disease management.(3)

Development of Recommendations

The methods used to develop the NAEPP guidelines are briefly described in the introduction of the EPR-2 report. A science-based committee of U.S. asthma experts, along with international members of the Global Initiative for Asthma was asked to examine all relevant literature and make evidence-based recommendations from their findings. When a clear recommendation could not be stated, or if the evidence was conflicting, the Panel was asked to indicate this in their recommendations.(3)

Document Preparation

Document preparation is also addressed briefly in the introduction. The report was prepared in a systematic and iterative process. The full report, '*Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma*' is available through the National Institutes of Health. Other reports that have been published in collaboration with the NAEPP guidelines include the *International Consensus Report on Diagnosis and Management of Asthma* (NHLBI) and the *Global Initiative for Asthma* (NHLBI/WHO).(3)

External Review

The EPR-2 report was funded entirely by the National Heart, Lung, and Blood Institute of the National Institutes of Health. Compensation for panel members was made only for travel expenses related to the expert panel meetings and the executive committee meetings. The EPR-2 review process consisted of two expert panel meetings, three executive committee meetings, one outside expert review, and two expert panel 'mail' reviews between June of 1995 and January 1997.(3)

2.5.3 NAEPP Asthma Guideline Components

The 1997 NAEPP asthma guidelines are divided into four major components. These are: (1) measurements of assessment and monitoring; (2) control of factors contributing to asthma severity; pharmacologic therapy; and (4) education for a partnership in asthma care. Each component of the 1997 guideline begins with a list of key points to be addressed, followed by the differences from the guidelines published by the 1991 Expert Panel Report. Below is a brief description of each component.

Component 1: Measures of Assessment and Monitoring

The first component, 'Measures of Assessment and Monitoring', is divided into two sections. The first section addresses the initial assessment and diagnosis of asthma while the second section is concerned with aspects of assessment and monitoring that are essential for asthma management. Recommendations regarding medical history, physical examination, pulmonary function testing, and additional studies, if needed, are made in

the first section of this component. Key points addressed in this section include: (1) establishing an asthma diagnosis (airflow obstruction, reversibility, and exclusion of alternate diagnoses); (2) mechanisms to make the diagnosis (medical history, physical exam, spirometry); and (3) other considerations of diagnosis (precipitating factors, severity, complications). The goals of asthma therapy are also described as key points. They include prevention of chronic and troublesome symptoms, maintaining normal pulmonary function, maintaining normal activity levels, preventing exacerbations, providing optimal pharmacotherapy, and meeting patient and family expectations regarding asthma care. The second section describes the necessary measurements to assess the effectiveness of asthma therapy. These include evaluations of the signs and symptoms of asthma, pulmonary function tests, the impact of asthma on quality of life, the number and severity of asthma exacerbations, and adjustments made to pharmacotherapy.

Other key points in this section describe the importance of patient-clinician partnerships for making asthma assessments, the value of spirometry in making asthma diagnoses, the disease management benefits of a written action plan for both the patient and clinician, and the advantages of teaching the patient to recognize signs and symptoms of inadequate asthma control.

Component 2: Control of Factors Contributing to Asthma Severity

The second major component of the asthma guidelines is the control of factors contributing to asthma severity. Recommendations in this section include methods for recognizing irritants and allergens and methods for reducing exposure to them. Specifically, for patients with persistent asthma, this section makes the following recommendations for clinicians: (1) identify allergen exposures; (2) assess sensitivity to seasonal allergens with patient's history; and (3) assess sensitivity to perennial indoor allergens with skin test. For patients with any level of asthma this section recommends the avoidance of: (1) allergens to which they are sensitive; (2) tobacco smoke; (3) exertion when levels of pollution are high; (4) use of beta-blocker; and (4) sulfite-containing foods.

Other key points address the need for medication counseling, vaccine use, and treatment for concurrent disease states.

Component 3: Pharmacologic Therapy

The third major component of the asthma guidelines is the pharmacologic management of asthma. The recommendations are based on disease severity as well as whether the condition is long-term, or an acute exacerbation of asthma. Regardless of the chronicity or severity of the disease, it is recommended that pharmacologic therapy be instituted in conjunction with environmental control measures to reduce exposure to allergenic factors. Additionally, long-term anti-inflammatory measures are emphasized by the

guidelines because of the early and persistent occurrence of an inflammatory component of the disease. The NAEPP goals of pharmacotherapy are the same as those listed earlier for Measures of Assessment and Monitoring (component 1) of asthma. In addition, this section addresses the role of pharmacotherapy in reducing asthma morbidity and mortality, the benefits of a stepwise pharmacologic approach to asthma therapy, the importance of regular followup visits to maintain control and monitor therapy, and some of the more recent medications. Georgitis, while lauding the expansiveness of the guidelines, states there are four areas in this section that need further clarification and discussion. They are: (1) safety and efficacy of the available asthma medications, (2) clinical efficacy comparisons of inhaled corticosteroids, (3) comparative risk among inhaled corticosteroids, and (4) expectations with different delivery systems used with inhaled corticosteroids.(157) As one of the characteristics of effective guidelines has been stated to be 'simplicity,' it is not certain whether adding this additional information would add or subtract from the usefulness of the guidelines. Certainly this information is available from other sources if deemed necessary to make a clinical decision.

Component 4: Education for a Partnership in Asthma care

According to NAEPP, the cornerstone for guideline based asthma management is the educational partnership between the health care providers and the patients. The guidelines recommend that education should start at the time of asthma diagnosis and be integrated into every step of clinical asthma care. Another key point of the guidelines is

active participation in the education process by all members of the health care team.

Concepts to be included and reinforced at every opportunity in this process include:

- basic facts about asthma;
- roles of medications;
- skills: inhaler/spacer/holding chamber use, self-monitoring;
- environmental control measures; and
- when and how to take rescue actions.

An additional recommendation of the NAEPP guidelines is a written daily self-management plan and an action plan for exacerbations. This is most critical for asthmatics considered to be moderate-to-severe and for patients with a history of severe exacerbations.

2.6 The Department of Defense Guideline Model

2.6.1 Overview

Until recently, attempts to implement Clinical Practice Guidelines (CPGs) at individual military facilities were rarely successful for the entire facility or for a long period of time.(158) Several recent developments in the U.S. Military Health System have begun to change this. The establishment of TRICARE in 1995 ushered in the managed care environment to military health. Prior to TRICARE, military hospitals and their branch clinics functioned as independent units. There was little interaction or coordination with the civilian health care provided through the Civilian Health and Medical Program of the Uniformed Services (CHAMPUS).(13) Under TRICARE, local Army, Navy, Air Force,

and Coast Guard hospital and clinic commanders now work together on a regional basis. A contractor is designated to manage both military and civilian health care for active duty members, their families, and those who retire from the service.(13) The current TRICARE network consists of eleven health service regions (HSRs) within the continental United States and three overseas regions, serving over eight million active duty, retirees, family members and survivors who are eligible for military health care. This network consists of 80 military hospitals and medical centers along with 513 clinics staffed by over 160,000 military health system personnel. In addition, the TRICARE network is augmented by over 161,000 providers in 2,000 civilian facilities and by over 28,000 pharmacies.(159) In a joint letter addressed to TRICARE stakeholders, J. Jarrett Clinton, Acting Assistant Secretary of Defense, and H. James T. Sears, Executive Director TRICARE Management Activity, outlined several objectives they felt necessary to ensure the continuation of the high quality of health for TRICARE beneficiaries. These objectives included improving access to care and increasing patient satisfaction, establishment of robust programs for active duty members and their families in remote locations, holding the line on costs, and enhancing the efficiency, productivity and service quality of all medical treatment facilities worldwide. Although by no means the only approach for achieving these goals, the use of guidelines certainly provide a framework from which to start.(159)

With the managed care environment of TRICARE firmly established, a second major impetuous for guideline use within the Department of Defense occurred as a result of

collaborative efforts between the Department of Veterans Affairs. Since 1998, the selection of guideline topics and the guideline development process have been under the joint auspices of the Veterans Health Administration (VHA) and the DoD pursuant to directives from the Department of Veterans Affairs Undersecretary for Health and the DoD Assistant Secretary of Defense, Health Affairs. The U.S. Army Medical Command Quality Management Office has been the center of the DoD initiative to develop and implement guidelines. Currently guidelines have been developed, or are in the process of being developed for asthma, COPD, CVD, depression, diabetes, dysuria, low back pain, post-deployment (Gulf-War Syndrome), pregnancy, and tobacco use cessation. The current DoD/VHS asthma guidelines update an earlier version published in 1997. Work on this updated guideline for the Management of Asthma began in November of 1998 with the convening of an expert panel consisting of participants from the DoD, VHA, and academia, and a team of private guideline facilitators. The professional make-up of this multidisciplinary team consisted of internists, family practitioners, pediatricians, pulmonologists, allergists, nurse practitioners, physician assistants, nurses, pharmacists and health educators. The current guideline consists of two sections: one on the management of asthma for adults and children six years and over and a second on the management of asthma for infants and children under six. The stated goal of these guidelines was to incorporate information from existing, national recommendations into a format, which would maximally facilitate clinical decision-making. In doing so, this initiative borrowed extensively from the NHLBI's National Asthma Education and

Prevention Program Expert Panel Report 2, *Guidelines for the Diagnosis and Management of Asthma*, published in July of 1997.(160)

Wherever possible, the process used to develop the DoD/VHA guidelines was evidence-based. In areas where the evidence was either conflicting or ambiguous, or where scientific data were lacking, the clinical experience of the expert panel was used to guide consensus-based recommendations. The National Library of Medicine's MEDLINE database was used to conduct the literature review, after which panel members performed a critical analysis of all relevant literature. To promote an evidence-type approach to the guideline development process, the quality of evidence was rated using a hierarchical rating scheme based on the one used by the Agency for Health Care Policy and Research. The DoD/VHA asthma guideline consists of two major sections with four modules each.(160) The first section addresses asthma management in adults and children over six years of age, while the second addresses the management of asthma in children under six years of age who cannot perform spirometry. The modules in each section are: (1) diagnosis and initial management, (2) treatment follow-up management, (3) emergency management, and (4) telephone triage management.

2.6.2 Implementation of DoD/VA Asthma Guideline

Considerable time and resources have been invested by the Military Health Service to ensure that TRICARE is highly efficient and effective as a health care program. In part, the TRICARE goals of achieving efficient and cost-effective standardization of care are

dependent on the successful adoption, implementation, and institutionalization of guidelines. Anchoring the use of guidelines into the DoD Medical Service culture has required an effective change strategy. Through a collaborative effort between the Army Medical Department (AMEDD) and the RAND Corporation, a manual for guideline implementation was developed to assist DoD medical treatment facilities 'institutionalize' guidelines. The name of this manual is: *'Putting Practice Guidelines to Work in the Department of Defense Medical System: A Guide for Action.'*(14) In developing this guide, the authors have drawn upon theory, published literature, and field experience to provide information, instructions, and examples for each of the major steps in guideline use. Numerous similarities can be identified between the suggestions in this 'Guide for Action' for the adoption, implementation, and institutionalization of DoD/VA guidelines and the eight-stage process for change described by Kotter.

2.6.3 DoD Guideline Development/Adoption

Stage 1: (Establishing a sense of urgency)

The cost associated with providing health care to beneficiaries, while not solely responsible, was perhaps one of the most influential factors leading to the restructuring of the MHS and the subsequent use of guidelines to deliver health care services. By 1996, it was estimated that 25 percent of the entire DoD budget was being utilized to provide health care services to its beneficiaries at a cost of over \$15 billion.(16) Additionally, the sense of urgency within the DoD guideline movement was driven by the military leadership's desire to standardize care and to achieve greater consistency, quality, and

cost-effectiveness in the delivery of their health care services.(14) Asthma was selected for the initial launch of the DoD/VHA guideline initiative based on its prevalence in the VHA and DoD populations, the health risks associated with this condition, and the mitigating effects that an early diagnosis and preventive treatment could have on the frequency and severity of asthma symptoms and mortality within the DoD/VA population.

Stage 2: (Creating a Guiding Coalition)

The establishment of a guiding coalition was necessary at two levels. First at the DoD level and second at the regional and MTF level.

DoD Level Efforts

The DoD/VA Guideline Adaptation Process: In early 1998, the DoD in collaboration with the VA, established a working group consisting of two members of each military service and the VA to develop a single standard of care for use in the military/VA environment. The goals of this working group were: (1) adaptation of existing clinical practice guidelines for selected conditions; (2) selection of two to four indicators for each guideline to benchmark and monitor implementation; and (3) integration of DoD/VA prevention, pharmaceutical and information efforts. To address 'disease specific' standard-of-care issues, the working group appointed expert panels consisting of members from each military service and VA to review existing national guidelines, along

with their corresponding evidence, and make adaptations for use within the DoD/VA health systems.(14)

The AMEDD/RAND Guideline Implementation Process: DoD level support for guideline implementation was provided the Army Medical Department (AMEDD)/RAND guideline implementation project. The goal of this project was to establish a system for implementing selected practice guidelines throughout the DoD and for monitoring the impacts of those guidelines on clinical care and outcomes.(14)

MTF Level Efforts

The successful implementation of guidelines at MTFs required the commitment of staff-time and resources that were generally already in short supply. The key to implementation was MTF commanders who were convinced that guidelines could provide benefits to the MTF and therefore were willing to support the program. Support of the MTF executive staff, department chiefs, and specialty experts or opinion leaders was also crucial to the process of developing a sense of urgency for the guideline process. Other than the MTF commander, perhaps the most influential person for ensuring the successful implementation of MTF guidelines was the clinical leader of the implementation team, otherwise known as the "guideline champion." This person set the tone for the implementation process, selected implementation team members, and had overall responsibility of implementation activities.(14)

2.6.4 DoD Guideline Implementation

The implementation phase of the guideline use process within the MHS corresponds closely to the strategies described in stages three to six of Kotter's theory for organizational change (Developing a vision and strategy, communicating the change vision, empowering broad-based action, generating short-term wins).

The MHS 'continuous improvement' guideline implementation process, as illustrated Figure 2.6, contains the following elements:(14)

- Evidence-based practice guideline and metrics: – The official DoD/VA practice guideline and monitoring metrics are provided to the MTFs.
- Guideline toolkit: - MEDCOM and the Center for Health Promotion and Preventive Medicine (CHPPM) collaborate in developing a toolkit of materials (e.g., documentation forms, provider training videos, patient education materials, reminder cards) to support the MTFs' guideline implementation activities.
- Off-site planning conference: - The MTF's guideline implementation team holds a one-day planning meeting to develop implementation strategy.
- MTF implementation activities: - The MTF teams carry out their action plans. Periodic reports are prepared to summarize recent activities, successes, challenges, and assistance needed to support their work.
- Information exchange: - The MTF implementation teams are encouraged to share their experiences and build on each others' successes.

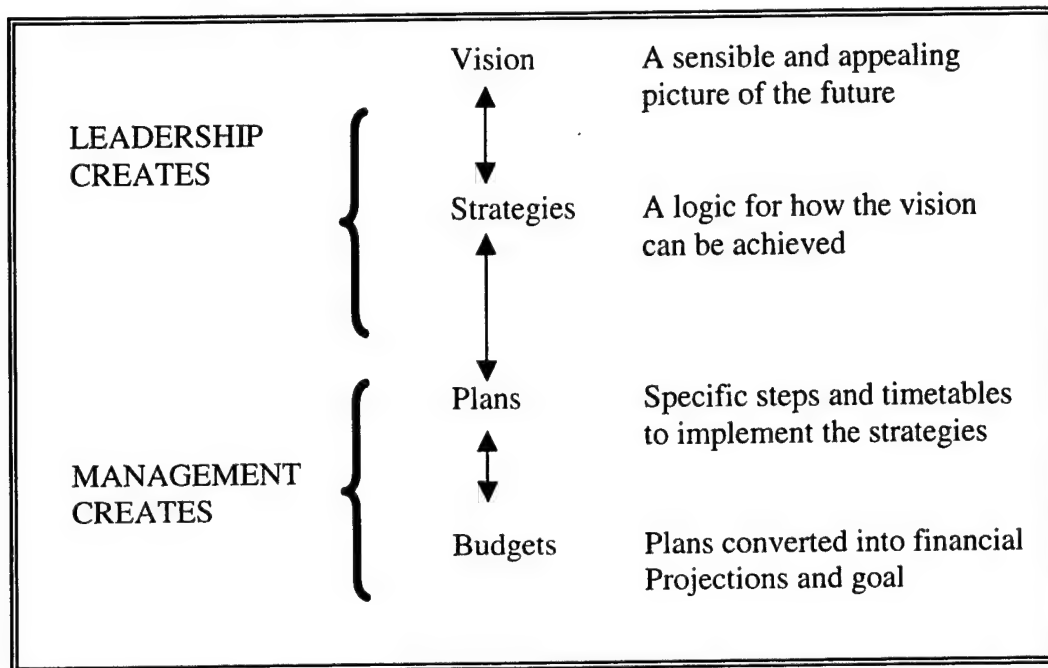
As in the adoption or development phase, the process of guideline implementation depends heavily upon leadership support for success. As noted in Figure 2.7, Kotter clearly places the responsibility of creating the 'vision' for change with the organization leadership. Referring back to Figure 2.6, the purpose of the off-site planning conference was to assemble together the pre-work conducted by the MTF implementation teams, the toolkit information, and the evidence-based guideline, in order to provide the MTF leadership with the information needed to form a compelling vision of medical care with guidelines.

The next step in the MHS guideline use process was a strategy for implementation. This step involved the development of a MTF action plan, supported not only by the MTF leadership, but also by the individual department managers.(114)

2.6.5 DoD Guideline Institutionalization

The seventh and eighth stages of Kotter's Theory for Organization Change correspond with the institutionalization phase of guideline use in the MHS. (Consolidating gains and producing more change, anchoring new approaches in the culture).

Figure 2.7: Kotter's Relationship of Vision, Strategies, Plans, and Budgets



Adapted from Kotter JP. Leading Change. Boston, Massachusetts: Harvard Business School Press; 1996

Kotter points out that consolidating gains and anchoring new approaches, such as guideline use into the military culture, depends on a number of factors - not the least of which is a clear indication that the proposed changes result in improvements to the processes or outcomes of interest. In the 'Guide for Action', the impacts of the 'guideline' process are determined through the use of a feedback loop. A primary component of the feedback loop is the use of metrics. Metrics are specific, measurable indicators designed to provide information about the status of an outcome. The information derived from monitoring metrics can then be used to make determinations regarding future implementation activities. This includes the possibility of modifying current implementation actions or even initiating new strategies. With every change

made to an implementation activity, additional information is generated which is subsequently fed back into the cycle for further metric feedback. In this way, implementation activities continue to be modified until the desired guideline outcomes or processes have been achieved. This allows for the clear documentation of the benefits achieved through the change process. According to Kotter, this is one of the most crucial aspects of the institutionalization process.(114)

Specific and well-planned steps are thus required for successful organizational change to occur. The approach used by the DoD MHS to implement guidelines was a multi-stage process, similar to Kotter's change theory, that addressed the development, implementation, and institutionalization phases of the change process. Overall success of the guideline use program depended on support both at the DoD level as well as at the military service, TRICARE region, and MTF levels.

2.6.6 Guideline Effectiveness - Improving Outcomes

The previous sections have discussed the organizational change issues involved with establishing guidelines as a method of delivering health care. According to Davis and associates, however, there is no point in implementing guidelines unless they have a positive effect on patient or health outcomes(148). Fox et al describes the guideline use process as a cascade of events that starts with the gathering of evidence, proceeds through development, dissemination, and institutionalization steps, and then, to be complete, must end with a measurable patient or health outcome.(161) According to Deutsch, guidelines

and disease management programs must be linked to outcome measurements.

Appropriate outcome measures can include morbidity, mortality, health status, quality of life, patient satisfaction, hospital utilization, appropriate use of patient services, and cost of care.(162) The literature is mixed regarding the effectiveness of clinical practice guidelines on improving patient or health outcomes. Two reviews have been published evaluating the usefulness of CPGs in improving patient outcomes.

Grimshaw and Russell reported that 55 of 59 published assessments of CPGs reported statistically significant improvements in the process of care. A further nine of eleven studies showed a significant improvement in health care outcomes such as lowered cholesterol levels in patients. Of these evaluations, 24 investigated guidelines for specific clinical conditions, 27 studied preventive care, and eight reviewed guidelines for prescribing or for support services. Randomized controlled studies as well as studies utilizing before-after, crossover, and time series designs were included in the review.(104) This review was not without criticism. Davis suggested that the results of the 55 studies reported by Grimshaw and Russell were variable, often weak or positive for only one of several possible outcomes. Furthermore, positive outcomes often reflected the intensity of the intervention; for example, the use of information-only approaches resulted in less change than more complex interventions.(148)

Another review reporting the effects of clinical practice guidelines on patient outcomes was conducted by Worrall and associates.(163) Thirteen studies between 1980 and 1995

were identified as meeting the criteria of dealing with clinical care issues and reporting results as patient outcomes. Of these, five studies reported modest improvements in patient outcomes. None of the studies was continued for long enough to measure any impact on mortality rates.(163)

Although the first NAEPP asthma guidelines have been available for over a decade, few studies have been published regarding their effectiveness in improving clinical or economic outcomes. A MEDLINE review of asthma using different combinations of the keywords 'guidelines', 'clinical pathways', 'outcomes', and 'effectiveness,' resulted in the identification of six applicable studies.(183, 184, 185, 186, 187, 188) Five of the identified studies utilized a before-after study design;(183, 184, 185, 186, 187) the other was a randomized controlled study.(188) Additionally, four of the five before-after studies utilized databases to extract data.(183, 184, 185, 186) One study used retrospective chart review techniques to extract relevant data.(187) The intervention in four studies was the implementation of modified forms of the NAEPP asthma guidelines, (183, 185, 186, 188) and in two studies the intervention was a locally developed asthma guideline.(184, 187) In five of the six studies, the results suggested an improvement in both intermediate indicators and outcomes with guideline use.(183, 184, 185, 186, 188) In three studies guideline use was associated with a decreased length of stay (hospital or emergency department) and a lower asthma hospital admission/readmission rate.(185, 186, 187) Two studies reported decreases in treatment cost with guideline use.(185, 186) Another study reported an increase in peak-flow (PF) measurements in the guideline

group and a decrease in delay to pharmacologic therapy.(187) Still another study reported that subjects in the asthma guideline group were more likely to receive asthma education and a controller medication upon discharge, than those in the non-guideline group.(186) In the sixth study, no difference was found between the guideline group and control group with respect to length of hospital stay and rate of readmission, and only small differences were found between the groups with respect to cost of therapy.(187) The results of these studies will be discussed in greater detail in section 2.8.

2.6.7 Summary of Theory

The primary purpose of the previous section was to describe the theoretical background for conducting this study. This included providing a description of the central issue of concern, an explanatory theory suggesting why the issue was present, and strategies for improvement. The section then described several general theories for bringing about organizational change, followed by a discussion linking organizational change to the guideline use process, and then specifically the use of guidelines in asthma therapy, and finally, guideline use for asthma in the MHS. The section was concluded by relating published reports of outcomes with the guideline use process.

2.7 Study Design and Data

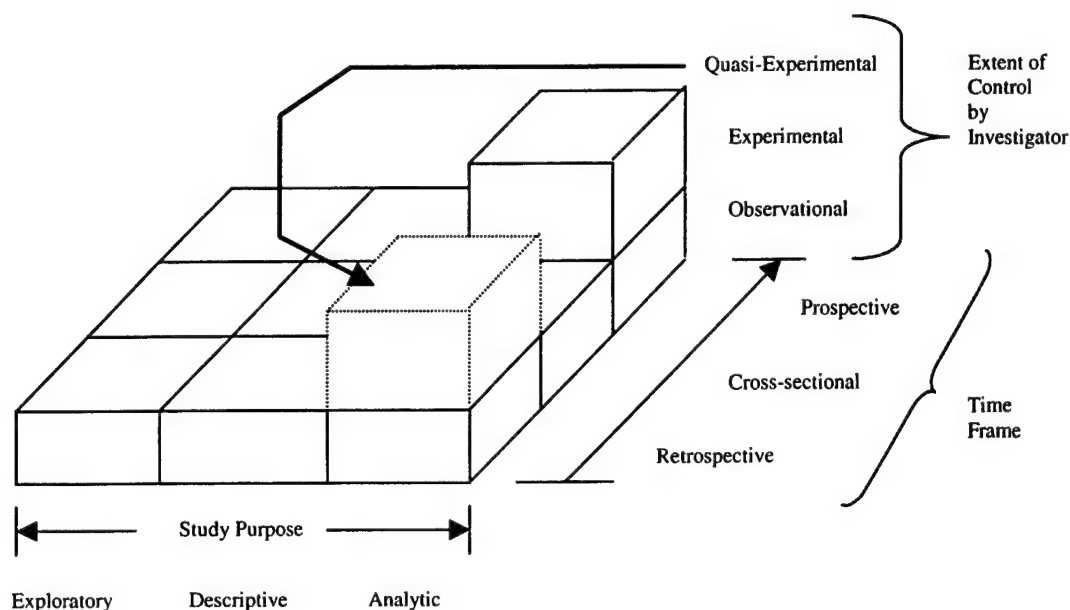
The purpose of this section is to provide a background for the study design and data used in this research, and to discuss the issues associated with each.

2.7.1 Before-After Study Design

Burkett provides a useful framework for understanding study design. He describes every study as being constructed along three axis. These are: (1) the objective or purpose of the study; (2) the time frame of the study; and (3) the amount of control the investigator maintains over the study activities. This study framework is illustrated in Figure 2.8.

Along the 'purpose' axis of this framework, the study design can be classified as exploratory, descriptive, or analytic. Likewise, there are three possible choices along the 'timeframe' axis: cross-sectional retrospective, and prospective. Finally, the axis describing the extent of control by the investigator can be classified as observational, experimental, or quasi-experimental.(164, 165)

Figure 2.8 Burkett's Framework for Study Design:



Adapted from: Burkett GL. Classifying basic research designs. Family Medicine 1990;22:143-148

Within the framework described by Burkett, a before-after study is almost always analytic because variables within the before and after groups are used to test a hypothesis. The timeframe of a before-after study can be retrospective, prospective, or in some cases a combination of retrospective and prospective. Before-after studies are not experimental because they lack one or more of the following properties: (1) manipulation – the experimenter does something to at least some of the subjects in the study; (2) control group – the experimenter introduces one or more controls over the experimental situation; and (3) randomization – the experimenter assigns subjects to a control or experimental group on a random basis. Depending upon the level of manipulation and whether a

control group is present, a before-after study can be classified as either observational or quasi-experimental.(166) Dotted lines are added to Burkett's framework to represent the quasi-experimental design.

Similarly to the standard pretest-posttest design described by Campell and Stanley, the study arms of the before and after design are constructed along different time lines.(167) In both designs the subjects are observed at some time before, and some time after the intervention of interest. The primary difference between the two designs is in the composition of the study groups. In the pretest-posttest design, the subjects observed pre- and post intervention are the same, constituting what is known as matched pairs. In the before-after design, although some matched pairs may be present, the rest of the subjects included in the pre- intervention group are independent of the subjects found in the post- intervention group. Because the groups in the pretest-posttest design are the same or 'matched', statistical techniques relating to a 'dependent group' design are required. On the other hand, because the groups in the before-after design are generally a mixture of dependent and independent subjects, it is often necessary to consider other statistical techniques. Depending on the proportional mixture of dependent and independent groups, several options may be employed. If the number of matched pairs in the sample is small compared to the number of independent subjects, it may be possible to conduct the analyses with independent statistical techniques by excluding the matched or 'dependent' component of the sample. If this option were followed, it would be necessary to provide a description of the excluded portion of the sample and discuss how

their inclusion may have affected the study results. On the other hand, if the majority of the sample is composed of matched pairs, then it might be possible to conduct the analyses with dependent statistical techniques by excluding the independent component of the sample. Again, the excluded group would need to be described and a discussion provided regarding how their inclusion may have affected the results of the study.

A third option for conducting the analyses would be to use a mixed group model. The advantage of this approach is that it allows all subjects to be included in the analyses. A mixed model is one that contains both fixed and random effects. When patient or treatment effects are assumed to be constant, they are considered to be 'fixed.' When the effects are assumed to arise from a probability distribution, they are considered to be 'random'. A mixed model allows the researcher to specify which effects are 'fixed' and which are 'random' when conducting analyses using statistical techniques such as regression models.

2.7.1.1 Internal Validity

Internal validity has to do with the internal fitness or rigor of a research design.(168) It asks the question – did the independent variable 'X' really produce a change in the dependent variable? Internal validity is concerned with controlling as many extraneous or irrelevant variables as possible so that alternative hypotheses regarding factors other than 'X' that could have contributed to the change in the dependent variable can be minimized or eliminated.(169) From an epidemiological framework, internal validity can

be described in terms of bias, and confounding. Last defines bias as a trend in collection, analysis, interpretation, publication, or review of data that can lead to conclusions that are systematically different from the truth.(170) Hennekens defines confounding as the mixing of effects between the exposure, the outcome, and a third factor that is associated with exposure and independently affects the risk of developing the outcome.(123)

Campell and Stanley delineate eight classes of extraneous or confounding variables that can threaten the internal validity of a research design. These include: history, maturation, testing, instrumentation, statistical regression, differential selection, attrition, and selection-maturation interaction.(167) With the exception of experimental mortality, the most effective method for controlling for these threats to internal validity is through random assignment.(168)

Since by definition, before-after studies do not make use of randomization as a control property, threats to internal validity can be problematic. The following factors can constitute a threat to the internal validity of a before-after study design as illustrated in Figure2.9.

Figure 2.9 Before-After Study Design

Before (Pretest)	Intervention	After (Posttest)
O ₁	X	O ₂

Contemporary history: History is of particular concern with the before-after study because of the use of a historical or external control group. As opposed to a randomized clinical trial, in which control group subjects are enrolled concurrently and in the same setting as subjects in the study group (internal controls), before-after studies are characterized by the use of sequential comparison groups in which the control group is taken from a previous period (external or historical control). Bailar et al point out that the temporal remoteness of the control group can substantially weaken the comparison to the treatment group.(171)

In the before-after study, the 'before' or control group always occurs at a time before the intervention, and prior to the 'after' group. The concern is that other events may occur between the first and second measurements, other than the experimental variable, that could influence the outcome of interest. Examples of this could be the introduction of a new asthma treatment policy other than the CPG under study, or the introduction of a new and effective pharmacologic agent into the treatment regimen.

The two most effective methods for minimizing the effect of history in a before-after study are: (1) decreasing the temporal distance between the before and after groups, and (2) adding an internal control group that covers the same time period as is covered by the comparator groups in the study (Figure 2.10). A short time span between the before and after measurements decreases the opportunity for other events to influence the effect on the dependent variable, and adding an internal control group allows the researcher to

control for any extraneous effects that do occur between baseline and the time the intervention takes place.

Figure 2.10 - Before-After Study Design with Parallel Control Group

Before (Pretest)	Intervention	After (Posttest)
O ₁	X	O ₂
O ₃		O ₄

Maturation, Testing Effects, Instrumentation, Mortality

Other threats that are relevant to the before-after design, according to Isaac, include maturation, testing effects, changing effects of instrumentation, statistical regression, and mortality.(169) As with 'history,' threats due to maturation and instrumentation can be minimized by reducing the time period between measurements in the 'before' and 'after' groups, and by using a parallel control group. Mortality is an issue in before-after studies primarily when the comparator groups consist of matched pairs and some of the subjects drop out after the intervention occurs. In cases where the comparator groups are independent of each other or mixed, mortality could become an issue if for some reason a certain type of subject was inadvertently dropped from the study after the intervention. For example, if one of the variables of an inpatient asthma study was disease severity, mortality could be an issue if, for some reason, a decision was made to close the hospital's emergency department (ED) during the 'after' phase of the study. This could

result in some of the more severe patients being excluded from analysis in the after group, since they may seek the services of another hospital with an ED rather than wait for an office appointment.

In addition to the above, Bailer discusses several other factors that may introduce confounding into a before-after study.⁽¹⁷¹⁾ Especially for studies involving disease states such as asthma, he suggests that seasonal variation could be an issue. For example, if the observations of an asthma study were collected at a time of the year when the pollen count was high in one arm of the study, but not the other, the differences observed between the groups may be due partially, or total, to the effect of the pollen in addition to effect of the 'X' of interest. In the same way, Bailer points out that variations in environment and geography can also create concerns regarding internal validity. In studies involving disease states, compliance issues can also be problematic, particularly if one treatment regimen is more complex than the other.

Bias issues can also affect the internal validity of a study. Bias may be defined as any systematic error that differs according to treatment group.⁽¹²³⁾ The two major types of bias include selection bias, which refers to errors that arise in the process of identifying the study population, and observation or information bias, which refers to any systematic error that occurs in the measurement of information.⁽¹²³⁾ As with other study designs, selection bias can be an issue in before-after studies. Selection bias can result from a number of circumstances related to the way in which individuals are ascertained and

selected for study. These include factors such as differential surveillance, diagnosis, or referral of individuals into the study.(123) Knowledge of the study hypotheses by individuals responsible for subject selection and allocation into groups has also been reported to result in selection bias.(172, 173)

The extent that observation bias occurs is often dependent on the type of data that is used and how it is collected. Recall and interviewer bias, although a concern in prospective studies involving patient interviews, are seldom a concern in database studies since data are recorded prior to the development of the study purpose. In database studies misclassification can be a concern. Misclassification is a type of observation bias that occurs whenever subjects are erroneously categorized with respect to either the independent or dependent variables of interest. The effect of misclassification depends on whether it is classified as differential or nondifferential. Nondifferential misclassification occurs when the proportions of subjects erroneously classified in the study groups are approximately equal, while in differential selection, proportions of misclassified subjects are different between study groups. Nondifferential misclassification, because it increases the similarity between the exposed and nonexposed groups, will move the true association between exposure and disease towards the null hypothesis. On the other hand, the observed effect of differential misclassification, depending on the particular situation, can be to biased in the direction of producing either an overestimate or underestimate of the true association.(123)

Beyond bias and confounding, there is always the possibility that an effect could be explained by chance. Hypothesis testing involves conducting a test of statistical significance to which sampling variability may be assessed to account for the results observed in a particular study. Although this process will not eliminate the role of chance in explaining a particular result, it does make it possible to quantify the role of chance.(123)

2.7.2 Use of Claims Databases for Outcomes Research

2.7.2.1 Database Definition

The Institute of Medicine (IOM) Committee on Regional Health Data Networks defined a database as “a large collection of data in a computer, organized so that it can be expanded, updated, and retrieved rapidly for various uses.”(174) Administrative or claims databases are the by-product of the process of delivery of healthcare services, such as reimbursing hospitals and physicians or determining individual eligibility for an insurance program. The information is aggregated by payers or governmental organizations for reimbursement, monitoring, or other payment-related purposes, such as hospital rate setting.(175)

2.7.2.2 Advantages/Disadvantages of Claims Database Use in Research

There are a number of benefits to using claims databases in health care research. These include an expanded scope of research opportunities, flexibility in defining variable parameters, and benefits in terms of study costs and statistical power.(176) Health-

system databases have also been found to be useful in providing descriptive statistics on disease states and for assessing the effectiveness of treatment regimens in real life situations.(177) According to Armstrong and Manuchehri, the greatest limitations to health-system databases relate to the quality and comprehensiveness of the data. This is because for most health care systems, the construct for collecting patient level data has more to do with billing and reimbursement issues than with health care research.(177) Other limitations, closely associated to problems of construct validity, are those related to issues of internal and external validity.(176)

Scope of Research Opportunities: Because of the link to a health care organizations payment system, claims databases are generally complete, meaning that a high proportion of all patient encounters or events in the target population appear in the database.(176) Additionally, because claims are generally an ongoing process, claims databases are often a good choice for conducting longitudinal studies, particularly for data collected from national populations that are typically demographically and geographically diverse.(178) Other benefits derived from the expanded scope of database research include their ability to examine large cohorts of subjects, patients with rare diseases, or very specific population subgroups. Additionally, databases allow examination of the real-world use of a treatment.(176)

Flexibility: According to Motheral and Fairman, another advantage of administrative databases is their methodological flexibility. Issues such as selection of control groups

and study periods are often easily manipulated. Additionally, changes to study designs or analysis procedures can usually be accomplished with relative ease. Along these same lines, ethical issues and intrusive procedures that sometimes accompany randomized studies are rarely encountered in database studies. Of further benefit is the fact that the research activities of database studies, by definition, do not affect the study outcome.(176)

Cost and Statistical Power: Compared to the manpower and time involved with a clinical trial, database research is considerably less costly and time consuming.(178, 179) In addition, statistical power is relatively easy to obtain due to the ability to abstract large numbers of cases.(176)

Threats to internal validity: A number of threats to internal validity are important to claims database research. One of particular concern is misclassification. As stated earlier, this is a type of observation bias that occurs whenever subjects are erroneously categorized with respect to either exposure or outcome status. In database research, misclassification can occur as a result of miscoding diagnostic information within the database. If miscoding occurs proportionally between the experimental and control groups it results in random or nondifferential misclassification with an underestimation of the true effect.(123) On the other hand, if miscoding causes misclassification to be unidirectionally related to the exposure-outcome relationship, it can cause the study to be systematically biased.(176)

One of the more common coding systems used in claims databases is the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM). This system is used to select populations for study, adjust for severity of diagnosis, assess complications of therapy, or identify claims of interest for cost determination. According to Armstrong, errors occur because of inappropriate documentation of diagnoses by physicians, improper selection of diagnostic codes by office staff, or keyboard errors during data entry.(177) Overcoding can occur accidentally or intentionally with the inclusion of more diagnostic codes than necessary to accurately reflect the patient's medical condition. Reimbursement systems such as diagnostic-related groups (DRGs) can influence coding due to the financial incentives of using one code over another. Undercoding can occur as a result of the provider not recording secondary diagnoses, insurance companies placing limits on the number of diagnoses that can be documented, or because a provider is hesitant to document a patient's disease state for insurance or other reasons.(180)

Threats to construct validity: Construct validity refers to the degree to which a variable accurately reflects the phenomenon that it purports to measure.(181) Quite often in database studies, variables are selected for reasons other than the purpose for which the study is being conducted, and the actual construct to be measured may not be available. In this case a proxy variable may be required to reflect the construct. An example would be the use of β -agonist inhalers in a prescription database to reflect a diagnosis of asthma.

If the proxy variable can be applied to a different construct than the one intended, this needs to be addressed as a threat to construct validity.

External Validity: Hulley and Cummings define 'external validity' as the degree to which conclusions are appropriate when applied to the universe outside of the study – in other words, it's the extent to which conclusions can be generalized to a broader population.(182) Factors that can affect the external validity of database studies include the characteristics of the study population (Medicaid, ethnicity, socioeconomic status, etc), plan designs (co-pays, formularies, etc), regional practice patterns, and cost differences.(176)

Other potential limitations to database research

Because of the high rate of change in corporate health care carriers, establishing eligibility in database studies can sometimes be problematic. According to Motheral and Fairman, not knowing the eligibility status of a subject makes it more difficult to attribute an observed effect to a specific independent variable.(176) If data are derived from a capitated environment, such as an HMO, much of the needed information may not be available directly from the billing and payment process.(176) Other things that should be considered when using claims databases are the potential for coding changes to have occurred over the course of the study period and the general lack of availability of clinical or humanistic outcomes.(176)

2.8. Previous Studies

As discussed earlier, there are six published studies that examined the impact of asthma guidelines on costs and quality of care. Five utilized a before-after design; one utilized a randomized controlled trial design. These studies are discussed below.

The results of a before-after study conducted by Emond and associates suggested that both intermediate indicators and outcomes improved with guideline use.(183) Using an adopted version of the National Asthma Education Program's clinical practice guidelines as the intervention, a 'before' group consisting of 51 adult asthmatics seen during January 1994, was compared with an 'after' group consisting of 145 similar patients seen during October 1994, February 1995, and June 1995. Data were compared across months using a nonparametric test for trend. Demographic and patient characteristics were similar across months. The following results were reported; initial peak flow (PF) measurements were obtained in 20 percent of patients before intervention, compared with 82 percent, 84 percent, and 83 percent during the post-intervention months (p for trend < 0.001).

Additionally follow-up PF readings improved significantly ($p < 0.001$) as did median delays to β -agonist and steroid therapy ($p < 0.001$ and $p < 0.04$ respectively). Outcomes improved, with median emergency department (ED) length of stay decreasing by 58 minutes ($p = 0.01$), and fewer inpatient admissions ($p = 0.05$). There was no improvement in the four-week hospital relapse rate. No data were collected in this analysis to evaluate economic outcomes.

The main limitations of this study were related to the research design (before-after), and the time frame (retrospective) for data collection. As discussed previously, one of the internal validity concerns of this particular design was the threat of history. The authors briefly addressed this in their discussion by stating "unmeasured confounders, such as other 'streamlined' initiatives, might have spilled over into asthma care efforts." Also, confounding due to seasonal variation was a concern because data collection for the before and after comparator groups occurred at different times of the year. Again, this was briefly addressed by the authors by stating that they found no differences in the "before" and "after" groups including a winter month when acute asthma incidence was low. Since data for both groups were retrospective it is unlikely that compliance differences between groups would be an issue unless greater emphasis was being placed on compliance over time as a result of guideline use. If this were so, then any benefit as a result of increased compliance should rightfully be measured as an effect of guideline use. Selection and information bias were not a large issue in this study because methods for subject selection and data extraction were consistent across comparator groups. Of concern to the statistical analysis of this study was the mix of subjects. No discussion was provided regarding whether the statistical techniques used were appropriate for matched subjects, independent subjects, or both.

Akerman and Sinert also reported that the use of guidelines improved outcomes in asthmatic patients treated at an inner-city emergency department.(184) In a before-after study, in which 19,802 consecutive adult asthmatics seen between July 1991 and

December of 1993 were compared with a historical control of 7,923 consecutive asthmatic patients, both monthly asthma relapse rates and monthly asthma readmission rates decreased significantly. After the implementation of an asthma guideline, asthma relapse rate dropped from 12.18 percent to 7.83 percent ($p < 0.001$) and the readmission rate dropped from 4.85 to 3.90 per 100 emergency room asthmatic visits ($p < 0.05$). As with the study by Emond et al., limitations to this study were primarily related to characteristics of the before-after design and the time frame over which the study was conducted. However, while it is unlikely that any new treatment modalities, other than those incorporated in to the guidelines, occurred within the study timeframe, it is plausible, considering the total length of the study (47 months), that other policy changes such as criteria for hospital admission, length of stay, or population served (e.g. change in insurance carriers), could have occurred. The potential for bias is also a major concern for this study. Awareness that a study was being conducted could have resulted in changes in the way data were either recorded or extracted in the prospective group as compared to how it was done for the historical control. As with the Emond et al study, the statistical issue of mixing subjects between the comparator groups was also a concern. No discussion was provided in the study in regards to this.

Wazeka and co-workers also reported improved asthma outcomes with guideline use in a before-after study conducted in a pediatric hospital environment.(185) In their study of children aged two to eighteen, hospitalized with a history or recurrent wheeze, the authors reported a significant decrease in length of hospitalization from 4.2 days to 2.7

days ($p < 0.0001$) with the use of guidelines. Additionally, they reported a significant decrease in total charges for pediatric asthma admissions (\$2 million to \$1.4 million; $p < 0.005$) as well as decreases in nursing and laboratory costs. The limitations associated with retrospective before-after designs addressed in the previous two studies also apply here. It should be mentioned however, that the authors did address several issues of confounding and bias in their discussion. For instance, they stated that both the population served and policies affecting hospital admission and length of stay remained constant over both study periods. Additionally, because the number of demographic variables collected in this research was limited, the authors reported that the generalizability of the results was also limited.

In another before-after study, Kelly et al. reported that length of stay was significantly lower in the clinical pathway group of hospitalized asthmatic children, compared with the control group (36 hours versus 71 hours, $p < 0.001$).⁽¹⁸⁶⁾ They also reported a decrease in total costs (\$1685 versus \$2829, $p < 0.001$) with the pathway group, along with an increased frequency of receiving asthma instruction (65% versus 18%, $p < 0.001$), and an increased chance of being discharged with a controller medication (88% versus 53%, $p < 0.01$). The internal validity issues discussed in conjunction with the previous before-after studies apply to this study as well. Additionally, observation bias may be a concern due to the use of retrospective chart reviews to abstract data. Unlike database studies, in which programming commands are applied consistently to variables of both groups, data taken directly from charts can be subject to the bias of the abstracters. An effective way

to control for this is to blind the abstracters from the study hypotheses. This was not discussed by the authors.

In the final before-after study identified in the literature search, Kwan-Gett and associates reported no improvements in five out of seven outcome measures recorded in a population of children admitted to a hospital for the treatment of asthma.(187) The intervention was a consensus-guideline locally developed by a team of nurses, community pediatricians, academic general pediatricians, pediatric pulmonologists, respiratory therapists, and other unspecified professionals using what was stated as 'best available' information. The clinical outcomes of interest were length of hospital stay and rate of readmission within 14 days of discharge. Resource utilization was analyzed using electronic billing records and included flowmeter use, laboratory studies, radiological studies, and respiratory therapy. The authors concluded that guidelines had no effect on the clinical outcomes of length of hospital stay or rate of readmission to the hospital and only small effects on resource use including the use of steroids and peak flowmeters. As with the studies discussed previously, the issues related to both retrospective and before-after study designs apply to this study. A summary of the characteristics of the before-after studies discussed, are presented in Table 2.8.

In addition to the above studies, one study not using a before-after design was identified. Using a randomized controlled trial design; Johnson and associates studied the effect of a change in guideline use on the management of 110 inpatient asthmatic children between

the ages of two and 18.(188) Prior to the change in guideline use, weaning of nebulized β -agonist therapy was done only after physician assessment of the patient. This raised two concerns for the researchers. First, was that the assessment was not standardized, making the weaning procedure subject to whatever approach was preferred by specific physicians. The second concern was that the weaning of an asthmatic patient off of a nebulized β -agonist agent was typically not a high priority for busy physicians, which frequently led to unnecessary delays in this function. The proposed guideline change hypothesized that using the registered nursing staff to evaluate and modify nebulized β -agonist therapy would improve the rate and consistency of weaning. Both outcomes of interest (patients' length of stay and use of nebulized β -agonist therapy while hospitalized) improved in the guideline arm of the study as compared to the control group. The duration of hospitalization was 13 hours less for patients managed according to the clinical pathway (53.7 versus 40.3 hours; $p < 0.01$) and β -agonist use decreased significantly as well. Because of the randomized, prospective, nature of this analytic design, many of the limitations inherent in an observational study, such as a before-after design, were not problematic in this study. Randomization is an effective control for most issues of internal validity with the exception of experimental mortality.(168) In this study, one of the inclusion criteria was the availability of an inpatient bed in either the intervention or control nursing units when an otherwise eligible patient was admitted. If no bed was available in either of these units, the patient was not included in the study. Of the 432 patients who met criteria to be enrolled in the study, 314 were admitted on days when a bed was not available on either unit. This left a total of 118 patients who were

eligible for the study. Of these, six did not wish to participate, and two disenrolled after randomization, leaving a total of 110 patients. This number represents only 26 percent of potential enrollees if bed availability was not considered. However, if only those patients for whom a bed was available are considered then the drop-out rate was only two percent. Although this was a strong study, it investigated only a limited aspect of guideline use in asthma. This limits its ability to generalize its results to a broader definition of guideline use.

Little has been published regarding the effect of asthma guideline use in the DoD. An ongoing quality management review collaboration between the RAND Corporation and the DoD has assessed and published the effects of guidelines on asthma outcomes, however the results of this assessment are not available for public disclosure.

Table 2.8 Characteristics of Before-After Studies Assessing the Effects of Asthma Guidelines

Study	Design	Population	Inter- vention	Outcomes measured	GL ^c effect	Time frame ^d	Timeline ^e	Mixed ^f sample possible	Unit of analysis (Before/After) Visits (7923/19802)
Akerman 1999	Before- after	Adult asthmatics	LDAG ^b	1. Asthma relapse rate 2. Hospital admission rate	Yes Yes	R/P	12-5-30	Yes	
Kwan- Gett 1997	Before- after	Hospitalized children older than 2 years of age	LDAG ^b	1. Peak flow meter use 2. Steroid use 3. Laboratory use 4. Radiology services use 5. Total Charges 6. Length of Stay 7. Rate of readmission	No No Yes Yes No No No	R	12-0-12	Yes	Visits (342/353)
Kelly 2000	Before- after	Hospitalized asthmatic children	Modified NHLBI guidelines	1. Length of stay 2. Total costs 3. Complete asthma teaching 4. Discharge with PF meter 5. Appropriate discharge meds	Yes Yes Yes Yes Yes	R/P	4-12-4	Yes	Patients (34/34)
Emond 1999	Before- after	Urban adult asthmatics seen in Emergency Room	Modified NHLBI guidelines	1. Process improvements 2. Rate of PF measurements 3. Rate of followup PF measures 4. Time to steroid administration 5. ED length of stay 3. Inpatient Admissions 4. rehospitalization within 4 weeks	Yes Yes Yes Yes Yes Yes No	R	1-8-1,1,1	Yes	Visits (51/145)
Wazeka 2001	Before- after	Hospitalized asthmatic children	Modified NHLBI guidelines	1. Length of stay 2. Total charges 3. Nursing costs 4. Laboratory cost 5. Hospital readmissions	Yes Yes Yes Yes Yes	R	12-0-48	Yes	Visits (206/1004)

^aED - refers to emergency department.

^bLDAG - refers to locally developed asthma guidelines.

^cGL effect - refers to a guideline effect significant at $p \leq 0.05$. 'Yes' indicates significance, 'No' indicates non-significance.

^dTime Frame - 'p' refers to a prospective design, 'R' refers to a retrospective design, 'P/R' refers to a mixed retrospective/prospective design

^eTimeline - refers to the number of months data were collected on the before group, the delay before beginning the intervention, and the number of months data were collected on the after group.

^fMixed sample possible - refers to the possibility that patients seen in the before group were also seen in the after group.

2.9 Summary of Literature Review

The literature suggests that asthma, despite the considerable resources that have been invested in research and treatment, continues to show increases in prevalence in the United States and around the world. Costs associated with asthma are also increasing, as are mortality and morbidity rates. For troop readiness purposes, maintaining healthy populations, and containment of costs, the DoD has an interest in the efficient management of asthma, both in its active duty force, and in its dependent and retired populations. A recent strategy by the DoD to manage asthma in their population, was to implement and institutionalize evidence-based clinical practice guidelines. The most systematic and complete asthma guidelines have been developed by the National Heart, Lung, and Blood Institute or the National Institutes of Health. They consist of four main components which include the initial assessment and diagnosis of asthma; the control of factors contributing to asthma severity; pharmacologic therapy; and the place of education in asthma care. Like many other health care organizations, the DoD in collaboration with the VA and contracting groups like RAND, have borrowed heavily from the NHLBI asthma guidelines for the development of their own version of asthma guidelines. Although in the past, guideline use within the DoD was inconsistently applied between the medical services, a more systematic approach for guideline application, including those for asthma, is currently underway under the leadership of the Army Medical Department (AMEDD) and the RAND Corporation. The goal of the AMEDD/RAND Guideline Implementation Project is to improve disease management (including asthma) throughout the DoD/VA health care network through the

standardization of guideline use. One of the criticisms regarding the use of guidelines has been that despite their wide use, and the considerable effort required for their development and implementation, very little research has been conducted to establish their effectiveness in terms of clinical and economic outcomes. Of the research that has been conducted regarding the effectiveness of guideline use in asthma, the most commonly used study design has been the 'before-after' design. The results of these 'before-after' studies suggest beneficial effects of guideline use for both clinical and economic outcomes. A concern of these studies however, is the numerous limitations associated with establishing strong internal validity with the 'before-after' design. These limitations are reflective of the difficulty in making cause-effect inferences with the use of data that is both observational and retrospective in nature. In spite of the limitations associated with observational designs, they are sometimes the best alternative available for conducting research. Quite often, study designs considered to have high levels of internal validity, such as randomized controlled studies, are often unable to be used in certain settings, such as the study of guideline effectiveness, due to ethical considerations.

Chapter 3: Methodology

3.1 Overview

The purpose of this research was to test the theory that standardized asthma treatment, based upon a formal guideline use process, would result in better outcomes than medical care delivered without formalized guideline standardization. Data for this research were analyzed, and results reported at the subject level. Measures evaluated included clinical and economic outcomes.

Specifically, the following research questions were addressed: (1) what is the association between guideline use and the direct costs of treating asthma; (2) what is the association between guideline use and the frequency of health care encounters for asthma (including prescriptions dispensed); (3) what is the association between guideline use and the frequency of health care visits for asthma (excluding prescriptions dispensed); (4) what is the association between guideline use and the risk of experiencing asthma exacerbations; (5) what is the association between guideline use in asthma and the number of prescriptions dispensed; (6) what is the association between guideline use and the length of asthma related hospital stays; and (7) what is the association between guideline use and the proportion of asthma patients who are prescribed long-term controller medications.

3.2 Study Hypotheses

Based on the above research questions, the following null hypotheses (H_0) were tested:

Ho: 1: There is no difference in the direct costs associated with asthma therapy between individuals treated before, and individuals treated after the implementation of guidelines.

Ho: 2: There is no difference, before and after the implementation of asthma guidelines, in the number of asthma related health care encounters for patients with a diagnosis of asthma.

Ho: 3: There is no difference, before and after the implementation of asthma guidelines, in the number of asthma related health care visits for patients with a diagnosis of asthma.

Ho: 4: There is no difference in the risk of experiencing an asthma exacerbation between individuals treated before guideline implementation and those treated after guideline implementation.

Ho: 5: There is no difference, before and after the implementation of asthma guidelines, in the number of prescriptions dispensed for asthma treatment.

Ho: 6: There is no difference in length of hospital stay (for a primary diagnosis of asthma) between individuals treated at MTFs before asthma guidelines were instituted, and individuals treated at MTFs after asthma guidelines were instituted.

Ho: 7: The proportion of asthma patients treated with long-term control medications does not differ before and after the institution of asthma guidelines.

3.3 Study Design

A before-after, matched-pair, observational design utilizing a retrospective administrative data set was used for this research. The study exposure was the institution of the DoD/VA asthma clinical practice guidelines (CPGs). Study participants were selected on the basis that they had received asthma treatment from an army MTF both prior to, and after implementation of asthma CPGs. The before (control) group consisted of subject observations recorded in the database between 1 January 2000 and 30 September 2000. The after (experimental) group consisted of patient observations recorded in the database between 1 January 2001 and 30 September 2001. The asthma CPGs were instituted at all Army MTFs in September of 2000, and for the purposes of this study, the implementation period was defined as the period between 1 October 2000 and 31 December 2000.

As was discussed in chapter Two, a before-after study is derived from different time lines. This can be problematic in controlling for extraneous factors that may have occurred in one time period but not the other. Because of this, an internal control group was included in the design. Isaac refers to this as a nonrandomized control-group pretest-posttest study design.(169) The subjects in the internal control group were selected using the same criteria, and over the same time period, as those in the before-after groups of the study. However the control group received their asthma care at Navy and Air Force MTFs. Neither the Navy nor the Air Force had a formalized process for implementing asthma CPGs during this period. Figure 3.1 illustrates, in its simplest form, the study design used in this research.

Figure 3.1 Study Design Schematic

	Before Group (Historical)	CPG Exposure (Intervention)	After Group (Experimental)
CPG Use Group (Army)	O ₁	X ₁	O ₂
Internal Control Group (Air Force & Navy)	O ₃		O ₄

3.4 Study Sample

Subjects were included in the CPG-use group if: (1) they were eligible to receive medical care through the military health system (2) had received care related to asthma (ICD-9-CM 493.0 to 493.9) at an Army MTF during both the before and after study periods (1 January 2000 to 31 September 2000 and 1 January 2001 to 31 September 2001), and (3) were between the ages of five and 40 years of age on 1 January 2000. Subjects for the internal control group were selected using the same criteria as above but from Navy and Air Force MTFs.

The potential sample size available for this research was determined using prevalence and population data from the literature. Total beneficiaries enrolled in the MHS (TRICARE) in 1998 were 5,135,259. Of these, 2,010,274 beneficiaries were enrolled in a military MTF with 853,143 being active duty personnel, 796,446 being dependents of active duty personnel, and 360,684 being retirees less than 65 years of age.(189) Only active duty

personnel and dependents of active duty personnel were included in the sample size estimation. Using estimates from the National Center for Health Statistics of the probable number of children less than five years of age, an additional 29,400 subjects were excluded, leaving an estimated population of 1,620,149.(190) Prevalence of asthma in the general population has ranged between three and seven percent however for this study, a conservative estimate of asthma prevalence of three percent was used.(19, 22, 23) This was done to reflect the recruitment standards of military personnel regarding those with asthma.(54, 191) The total estimated number of asthmatics in this population was 48,604 in 1998.

3.5 Internal Validity Issues

As discussed in Chapter Two, analyses using a before-after study design have a number of internal validity issues that can present difficulties when trying to establish cause and effect relationships between dependent and independent variables. In an earlier work, Slack and Bennett developed a paper and pencil tool to assist in the identification and control of potential internal validity issues associated with before-after studies designs, specifically those used in investigating the impact of guidelines.(165) Elements of this tool (Appendix B) were employed in both the design and analysis phases of this study as a method to improve internal validity. A brief discussion regarding measures taken to identify the unit of analysis and control for bias and confounding is given below.

3.5.1 Unit of Analysis

Important to the issue of internal validity in before-after studies is an *a priori* statement concerning the unit(s) of analysis to be used in the research. All hypotheses in this research were tested using the subject as the unit of analysis. To obtain patient level data, observations for all variables associated with a unique patient identification number were collapsed into summary records.

3.5.2. Bias issues

In a before-after design utilizing a large administrative database, such as the one used in this research, it would be expected that there would be three groups of subjects: those that appear only in the 'before' group, those that appear only in the 'after' group, and those that appear in both the 'before' and 'after' groups. Because the intent of this study was to evaluate the effects of CPG use at the patient level, only subjects that appeared in both the 'before' and 'after' CPG exposure groups were included in the study. In this way, the effects that occurred at the subject level could be analyzed and reported.

A potential problem of limiting the analyses to matched pairs is that the results may be biased towards the sicker patients. This is because the appearance of a subject in both the before and after group may be indicative a more severe disease status, requiring multiple health care visits for treatment, as opposed to a less severe disease status in which sufficient treatment may be received in one health care visit. For the purpose of generalizability, the demographic characteristics of the subjects in the matched and unmatched groups were examined and compared using descriptive statistics. The more it

can be demonstrated that the demographics of groups are similar, the easier it is to generalize results between the groups.

The use of retrospective administrative data helps minimize several types of selection bias that can be problematic in prospective research. For example, variable coding in retrospective research is usually done prior to establishing a research question, and by a disinterested person. This minimizes the risk that selection bias will occur during the coding stage of the research. Additionally, there is little chance for comparator groups to be treated differently in this type of research since the same data commands are usually applied in the same manner to each group.(165)

Misclassification is another form of bias that can be associated with database analyses. It was minimized by carefully describing the variable selection process among comparator groups. Further, to the extent that misclassification did occur, it most likely occurred nondifferentially and in equal proportions among facilities. This type of misclassification affects each comparator group similarly and tends to bias the results towards the null.(123)

The potential for systematic bias in asthma severity due to differences in recruitment and retainment standards between military services was a concern. However, since the majority of individuals included in this study were dependents of active duty and,

therefore, not subject to military standards for recruitment and retainment, these issues would have less effect.

3.5.3. Confounding Issues

The potential for the occurrence of confounding in these analyses was also considered.

Confounding involves the possibility that the observed association between two variables is due, totally or in part, to the effects of differences between study groups other than the variable under study.⁽¹²³⁾ Several potential confounding issues were addressed.

Seasonal and environmental variations in asthma treatment were minimized by including MTFs from different geographical areas in each comparator group, and by defining the time periods of all comparator groups to be of similar length (nine months). The existence of a system-wide core formulary in the DoD helped to ensure similar resources were available at all MTFs, thus reducing resource variation as a confounding issue.

Historical threats to internal validity can also give rise to confounding concerns in before-after studies. The effects of this threat were minimized by keeping the time interval between the before and after groups as short (3 months) as possible and including an internal control group. Fortunately, no major policies or treatment modalities regarding asthma therapy, other than guideline implementation, were introduced within the DoD during the time period of this research.

Another potential confounding factor in this study was the possibility that physicians were receiving education apart from the CPG-use process and that this education was changing the way providers treated asthma subjects. There are several potential sources of post-graduate provider education. These include, but are not limited to, continuing education programs sponsored by the pharmaceutical industry, pharmaceutical representative promotional calls, local, regional, national, or international symposia, and articles appearing in printed media. There was no way to control for these factors given the available data.

Other sources of confounding such as age, gender, and branch of service were controlled by including them as variables in the analyses.

3.6 Data Source

The sources of data used in these analyses were retrospective administrative databases obtained from the Department of Defense Pharmacoeconomic Center (PEC). The PEC is a tri-service (Army, Navy, Air Force) organization that focuses on improving the clinical, economic and humanistic outcomes of drug therapy in support of the readiness and managed care missions of the Military Health System (MHS).

Specifically, databases used in this study included the Uniform Services Pharmacy Data Set (USPD), the Standard Inpatient Data Record (SIDR), and the Standard Ambulatory Data Record (SADR). These data capture health care information from TRICARE, the health care program used by the Military Health System. Military MTFs are the main

delivery system of TRICARE with augmentation of services occurring through a civilian network of providers and facilities. TRICARE supports over eight million active duty, retirees, family members and survivors who are eligible for military health care. The military component of TRICARE consists of 80 military hospitals and medical centers and 513 clinics staffed by over 160,000 Military Health System personnel. The civilian TRICARE network consists of over 161,000 providers utilizing over 2,000 medical facilities and 28,000 pharmacies.(159)

Uniformed Services Prescription Database (USPD)

The USPD is a data warehouse of prescriptions dispensed to U.S. Military service members, dependents, and retirees from Military Treatment Facilities (MTFs) as recorded by individual Composite Health Care System (CHCS) sites. Prescription records, with encrypted patient and provider identifiers, are transferred to the Pharmacoeconomics Center (PEC) using industry-standard file transfer protocol. Edits are applied to the prescription records to validate, code, and consolidate the data for research and analysis in a SAS dataset located in the file systems of the Center for Health Education and Studies (CHES) at Ft. Sam Houston, Texas. Prescription fields captured by the USPD database include the name and social security number of the person for whom the medication was dispensed, the name of the medication, the date the medication was dispensed, instructions for use, quantity dispensed, number of authorized refills, providers specialty, branch of service of patient, dispensing MTF, eligibility status of patient, and other demographic and cost related fields. Prescription information from the

individual CHCS sites is added to the USPD on a weekly basis. Because the USPD database is a central database, drawing data from throughout the DoD, medications can continue to be tracked even if a patient is relocated to another duty assignment covered by a different MTF. For this reason it is believed that most of the medication data were captured by the USPD database.

Standard Ambulatory Data Records (SADR)

The Standard Ambulatory Data Record (SADR) is an electronic administrative database used by the Military Health Service to uniformly collect ambulatory care data across the medical services of the Army, Navy, and Air Force. Military health service data elements are entered into the SADR on a monthly basis, including demographic, diagnostic, and procedural codes from military and civilian treatment facilities worldwide

Standard Inpatient Data Records (SIDR)

The Standard Inpatient Data Record (SIDR) is an electronic administrative database used by the Military Health Service to uniformly collect hospitalization data across the medical services of the Army, Navy, and Air Force through the use of standard ICD-9 codes.(192) Data elements comparable with those in Medicare Part A files are entered into the SIDR on a monthly basis, including demographic, diagnostic, and procedural codes from inpatient admissions in military treatment facilities worldwide.(193) Meyer et al concluded the SIDR database to be a reliable source of administrative data (κ-

statistics ranging from 0.55 to 0.96) when compared to a database abstracted from clinical data (Civilian External Peer Review Program [CEPRP]).(193)

All Region Server (ARS) Bridge

SIDR and SADR data is made available through the All Region Server Bridge (ARS-Bridge). The ARS-Bridge is an initiative of the Executive Information/Decision Support Program Office (EI/DS), in conjunction with the TRICARE Management Activity Health Program, Analysis, and Evaluation (HPA&E) Branch, to summarize and consolidate military health care data into a central database.(194) As with the USPD database, the ARS-Bridge captures data from throughout the MHS, facilitating the capture of data even if patients are transferred between MTFs. The richness of both the demographic and the diagnostic aspects of the SIDR and SADR data sets make abstraction of data from the ARS-bridge an ideal choice for comparing medical treatments across the military medical services. For this reason, permission was sought and granted, from the PEC in San Antonio, Texas, to use these data sets to evaluate the effectiveness of clinical practice guidelines for the treatment of asthma in a military environment.

Merged Data Set

Data for this research was received from the PEC in the form of four compact disks. One disk contained the inpatient and outpatient SIDR and SADR (ARS-Bridge) data for the entire study period, while the remaining three disks each contained one calendar year of USPD pharmacy data. The common variable in each data set was a unique identification

number based upon the subject's scrambled social security number. In order to comply with the requirements of the Human Subjects Protection Program, all personal identifiers such as subject name, telephone number, or home address, were omitted in the databases. Data were converted from Microsoft Access® to SAS® using DBMScopy®. Data manipulation and variable formation within the dataset were done using SAS. Statistical analyses were conducted using SAS and STATA®. The variable used to merge data sets was the unique identification number of the subject.

3.7 Coding Issues in the Military Health Services Administrative Data Bases

As with much administrative health care research, the ICD-9 codes were an invaluable tool for the identification of specific disease states within the MHS database. Both the SIDR and SADR databases had fields for at least four levels of ICD-9 diagnoses. Subjects for this research were required to have an ICD-9 code between 493.0 and 493.9 within the first three diagnostic fields. Another common variable found in many administrative databases, including the SIDR/SADR is the current procedure terminology (CPT) code. These codes could be beneficial in determining the procedures that have been used during a treatment process, and subsequently, the costs of the treatment process by linking the procedures with a cost source like the health care financing agency. In addition to CPT codes, the SIDR and SADR databases included a data field for enrollment based capitation (EBC) cost. It represented the average cost of providing care in a specific MTF cost center, such as the emergency department. EBC costs, rather than costs derived from CPT codes, were used to calculate procedure and physician costs

in this research because of their specificity for MHS costs and their availability in the database.

Another important code in the MHS databases was the Medical Expense Performance Reporting System (MEPRs) code. This is a standardized code used to identify MTF cost centers. The MEPRs code transcends military service type such that a code assigned to care given within a cost center at one MTF, will be the same as the code assigned for care given in a similar cost center at any other MTF, irrespective of military service type or geographic location. For example, a MEPRs code of BIA, whether originating from F.E. Warren USAF Hospital in Cheyenne Wyoming, or at the Naval Medical Center in Portsmouth Virginia, was used to designate care received in an emergency department. In this research the MEPRs codes were useful in determining the departments responsible for providing asthma care.

The USPD database provided many useful variables. Those of greatest benefit to this research were the prescription fill date, the generic name of the prescription, the location the prescription was filled, and the prescription cost.

3.8 Statistical Analysis

This section provides a description of the dependent and independent variables used in the research analyses, and the statistical techniques used to test the association between them. In addition, potential interactions between variables are described.

3.8.1 Variable Selection

All variables used in these analyses were obtained from the dataset formed by the merger of elements of USPD and SIDR/SADR (ARS-Bridge) data or were otherwise derived through manipulation of variables within this composite dataset. A list of the dependent variables used in these analyses is presented in Tables 3.1. The variables included in the complete dataset provided by the PEC are presented in Appendix D.

3.8.2 Dependent Variables

Two alternative approaches were considered for defining the dependent variables in this research. The first was to use the mean difference between variables in the periods before and after CPG exposure as the dependent variable; the second was to use the mean value of the outcome variables in the period after CPG exposure as the dependent variable while controlling for the mean value of corresponding variables in the period before CPG exposure by including them as independent variables. The latter approach was the method selected for this research.

One dependent or outcome variable was specified for each hypothesis. These included: 1) direct cost associated with asthma; 2) total asthma health care encounters; 3) health care visits for asthma; 4) asthma related prescriptions dispensed; 5) asthma related exacerbations; and 6) the number of asthma related beddays. The following paragraphs provide a detailed description of how each dependent variable was calculated.

- Direct costs of asthma care: For the purpose of this study, direct costs were limited to: (1) physician costs, (2) medication costs, and (3) hospital costs. Physician and hospital costs, which included visits to offices and clinics, hospital outpatient departments, and emergency department visits, were calculated by isolating asthma visits through the use of ICD-9 codes, and then summing the respective EBC costs associated with each visit. An EBC cost field was included in both the SIDR and SADR datasets provided by the ARS-bridge. Medication costs were calculated in two steps. First, using the medication name field in the USPD database, prescriptions dispensed for asthma medications (Appendix A) were identified and selected from each subject's composite medication profile. Second, total medication costs were calculated by summing the cost field for all identified asthma prescriptions.
- Number of health care encounters associated with asthma: This was calculated as the sum of all asthma related health care encounters that occurred per patient, over the course of the study period. This included inpatient and ambulatory encounters as well as total number of prescriptions. Asthma related encounters were defined

as a visit with an ICD-9 code between 493.0 and 493.9 associated with one of the first three diagnoses. Prescriptions were counted if they were dispensed for any medication listed in Appendix A.

- Number of visits to a health care provider attributed to asthma care: As with encounters, this variable was calculated as the sum of all asthma related health care visits that occurred per patient over the course of the study period. As with the prior variable, ICD-9 codes between 493.0 and 493.9 were used to identify visits. This variable is different from health care encounters in that it does not include prescriptions.
- Number of prescriptions dispensed: This variable was calculated as the sum of all prescriptions associated with the treatment of asthma that were dispensed to a subject over the course of the study period. This information was abstracted from the USPD database. Appendix A lists the medications included in the calculation of this variable.
- Number of asthma exacerbations: The number of asthma exacerbations was calculated by summing all hospital admissions and emergency department or acute care visits containing a primary diagnosis of asthma during the study period. Identification of the primary diagnosis was done using ICD-9 codes between 493.0 and 493.9. Emergency room or acute care visits were identified using the MEPRs three digit code of BIA.

- Number of bed days: The number of bed days associated with asthma related hospital admissions was determined using the SDR variable 'Bed Days, Raw' for subjects with a primary diagnosis of asthma.

A summary of the dependent variables used in this research is presented in Table 3.1:

Table 3.1 Dependent Variables (Determined from data in period after CPG implementation)

<i>Dependent Variables</i>	<i>Variable Name</i>	<i>Variable type</i>	<i>Variable Categories</i>	<i>Hypothesis number</i>
Direct cost of asthma therapy	TCA	Continuous		1
Asthma related health care encounters (includes Rx's)	T_E_A	Continuous		2
Asthma related health care visits (Rx's excluded)	TA_Visit	Continuous		3
Asthma exacerbations	TA_Exac	Dichotomous	0 – Exacerbations 1 – No exacerbations	4
Total number of prescriptions	RxAfter	Continuous		5
Length of hospital stay	Bed_A	Continuous		6

3.8.3 Independent Variables

Ten independent variables were included in these analyses. They were CPG use, MTF size, MTF service type, gender, age, rank of sponsor, ethnicity, TRICARE region, duty status, and the presence or absence of respiratory comorbidity. A description of each is provided below:

- Clinical Practice Guideline Use: A dichotomous variable (cpg) was used to indicate the presence or absence of a formalized CPG use process for the treatment of asthma. For the purposes of this research, a formalized CPG process

was defined as a command-directed program which only includes Army facilities.

A value of one was assigned to the variable for subjects in the CPG-use category (Army) and a value of zero for those not in the CPG use category (Air Force, Navy, other).

- MTF Size: A categorical variable (fcats) was included in each analysis to control for potential effects of facility size on the outcomes of interest. Six categories were specified based on the number of total observations occurring in the database for each facility: (1) one to 250; (2) 151 to 500; (3) 501 to 1000; (4) 1001 to 2000; (5) 2001 to 3000; and (6) greater than 3000.
- TRICARE Region: A categorical variable (region1), consisting of TRICARE Regions one through 13, was used to control for outcome variance between TRICARE regions. Region one, consisting of states in the upper north-east part of the country, including MTFs in the Washington DC area, was selected as the referent group. The TRICARE region in which a MTF is located may be relevant to the success of CPG implementation. The military health care system is divided into eleven regions within the continental United States and three outside the North American continent. Each TRICARE region has one facility, called the Lead-Agent, which is responsible for administering health care policy and allocating health care resources for the entire region. The success of CPG implementation may be associated with the amount of administrative support and

resource allocation received by a specific MTF from the Lead-Agent of their region. TRICARE regions are listed in Table 3.2.

- Facility type: Two variables were included to differentiate the effect of CPGs between facility types. A categorical variable (F_Type) for medical service type was included in each analysis to control for the impact of MTF service type on the outcomes of interest. The four types were: (1) Army, (2) Navy, (3) Air Force, and (4) other. The reference category for this variable was the Army since it was the service with the formalized CPG implementation process. Another categorical variable (L_Agent) was included to control for differences between the Lead Agent MTF (1) and the other MTFs (0) in the TRICARE region. Since the MTFs other than Lead Agent facilities made up the majority of MTFs, they were considered the reference group. Lead agent facilities are listed in Table 3.2.

Table 3.2: TRICARE Regions and Lead Agent MTFs

<i>Region</i>	<i>Area</i>	<i>Lead-Agent MTF</i>
Region 1	Northeast	Walter Reed Army Medical Center
Region 2	Mid-Atlantic	Naval Medical Center, Portsmouth, VA
Region 3	Southeast	Eisenhower Army Medical Center, Ft Gordon, GA
Region 4	Gulfsouth	81 st Medical Group, Keesler AFB, MS
Region 5	Heartland	74 th Medical Group, Wright Patterson AFB, OH
Region 6	Southwest	Wilford Hall Medical Center, Lackland AFB, TX
Region 7/8	Central	Fort Carson, CO
Region 9	Southern Calif	Naval Medical Center, San Diego, CA
Region 10	Golden Gate	David Grant Medical Center, Travis AFB, CA
Region 11	Northwest	Madigan Army Medical Center, Tacoma, WA

- Age: To examine the impact of age on the dependent variables, a categorical variable (age_cat) consisting of three groups, five to 12 years, 13 to 18 years, and

19 to 40 years was created. The age range in each group was chosen to represent the three major divisions of subjects included in the study: children, adolescents, and adults respectively. No subjects under the age of five, and beyond the age of 40 were included in the study for the following reasons. In children under five years of age, it is often difficult to establish a reliable diagnosis of asthma due to difficulties with communication and obtaining reliable spirometry measurements.(195) For those over the age of 40, retirement and second-career opportunities make it difficult to ensure that the MHS will continue to be used for health care services. Since it would be expected that children would comprise a large portion of asthmatics in the DoD population, this group was selected as the reference category. This variable was included to control for potential age-related effects on the dependent variables. For instance, not only is a different set of asthma CPGs used for the extremely young asthma subjects treated at DoD MTFs, but CPG recommendations for treatment, including medication dosing, varies within guidelines by age.

- Gender: This variable was included as a potential confounder because of evidence in the literature suggesting that asthma prevalence differs by gender.(196) Additionally, although the treatment outlined in the DoD guidelines for asthma is similar between males and females (except during pregnancy), issues like compliance and health care utilization patterns have been shown to differ by gender.(197) A dichotomous variable for gender (sex) was abstracted

off of the ARS-Bridge, and included in each analysis with the reference category was female.

- Multiple Facilities: This variable was included in the model to provide a method of comparing outcomes based on whether asthma care was received from one facility or more than one facility. Facility sites were defined as MTFs in which either inpatient or ambulatory care was received. If prescriptions were filled at a site other than where care was received, this was not considered as a change in facility.
- Duty Status: This variable was included in the models to provide a method of comparing outcomes based on subject's current participation status with the DoD. This was a categorical variable (F_bencat) stratified into the following four groups: (1) dependent active duty, (2) retired, (3) dependent of retired, and (4) active duty and guard. Although it was expected that the retiree/retiree dependent category would be small because of the five to 40 year age range defined in the inclusion criteria, it was necessary to include this category to account for individuals who had: (1) an enlistment date prior to their 20th birthday and, therefore, were eligible for retirement before their 40th birthday, or (2) upon retirement, had a spouse who was less than 40 years of age. Because it was expected that dependents of active duty would comprise the largest group in this category, it was used as the reference group.

- Respiratory Comorbidities: Another explanatory variable considered in these analyses was the presence of respiratory comorbidities. Although the presence of any comorbidity could potentially complicate the use of guidelines to treat asthma, comorbid respiratory diseases are especially problematic. First, they have the potential to complicate the diagnosis of asthma, and second, they can have an influence on disease severity.(21) In both circumstances, type and duration of therapy may be altered. Respiratory diseases identified by Brandman as being important comorbidities with asthma were used in these analyses.(198) A dichotomous variable (comd) was included to represent the presence or absence of any (chronic or acute) comorbidity. Another dichotomous variable (comd1) was used to test the effect of only chronic comorbidities on each of the dependent variables. Table 3.3 presents the comorbidities included in this research along with their respective ICD-9 codes.(198)

Table 3.3 Respiratory Comorbidities Associated with Asthma

<i>Types of Comorbidity</i>	<i>ICD-9 Diagnosis Code</i>
Acute	
Sinusitis	461.xx
Upper Respiratory Infection	465.xx
Bronchitis	466.xx
Allergic Rinitis	477.xx
Pneumonia	480.xx-486.xx
Otitis Media	381.xx
Chronic	
Sinusitis	473.xx
Bronchitis	490.xx-491.xx
COPD	496.xx

- Military Service Branch of Subject: Considerable resource sharing occurs in the MHS between the military branches. A categorical variable (svc) was included to designate the branch of service the subject was associated with while receiving care at an MTF. The four types were: (1) Army, (2) Navy, (3) Air Force, and (4) other. The reference category for this variable was the Army since they were the service with the formalized CPG implementation process.
- Socioeconomic Status - Although there is evidence to support the theory that lower socioeconomic status (SES) is associated with increased risk of experiencing asthma symptoms, the fields in the MHS datasets that would have been useful for defining this variable (i.e., service member rank and ethnicity) were largely unpopulated.(26) This variable was, therefore, not included in these analyses.

Independent variables are presented in tabular form in Table 3.4.

Table 3.4 Independent Variables

<i>Independent Variable</i>	<i>Variable Type</i>	<i>Categorical Values</i>
Guideline use (cpg)	Dichotomous	1 - Yes 2 - No
MTF Size (f_cat)	Categorical	1 - 1 to 250 observations 2 - 251 to 500 observations 3 - 501 to 1000 observations 4 - 1001 to 2000 observations 5 - 2001 to 3000 observations 6 - > 3000 observations
MTF Type (F_Type)	Categorical	1 - Army 2 - Navy 3 - Air Force 4 - Other
L_Type	Dichotomous	1 - Lead Agent Facility 2 - Other facility
Gender (sex)	Dichotomous	1 - Male 2 - Female
Subject Age (age_cat)	Categorical	1 - 5 to 12 yrs 2 - 13 to 18 yrs 3 - 19 to 40 yrs
TRICARE Region (otmtreg)	Categorical	1 - 13 (See table 3.2)
Multiple Facilities (mult_F)	Dichotomous	1 - Treatment at one facility only 2 - treatment at multiple facilities
Duty Status (F_bencat)	Categorical	1 - Dependent of active duty 2 - Retired 3 - Dependent of retired 4 - Active duty and guard
Respiratory Comorbidities (comd)	Dichotomous	1 - Yes 2 - No
Military Service branch of Subject (svc)	Categorical	1 - Army 2 - Navy 3 - Air Force 4 - Other
Total Encounters in before group (T_E_B)	Continuous	
Total visits in before group (Tbvisit)	Continuous	
Total cost in before group (TCB)	Continuous	
Total exacerbations in before Group (TB_Exac)		
Total Rx's dispensed in before period (RxBefore)	Continuous	
Total number of beddays in before period (Bed_B)	Continuous	

3.8.4 Interaction Variables

In addition to the explanatory variables already defined, two interaction terms were considered. These were an interaction between age and gender and the interaction between comorbidity and gender.

As mentioned previously, in addition to the independent and interaction variables specified above, each analytic model included an independent variable consisting of the mean value of the variable in the period before CPG exposure, that corresponded to the variable used as the dependent variable.

3.8.5 Exploratory Analysis

The first step of the analysis was a visual review of the data dictionary to determine variable grouping. Descriptive statistics were then used to identify out-of-range variables, values with logical inconsistencies, and missing values. Correlations among continuous variables were determined with the use of scatter-plots, and the crosstabs function was used to examine the cell size for categorical data. Bivariate analyses between the dependent and independent variables were not conducted since the purpose of these analyses was explanatory and not predictive. Missing data were assumed to be missing completely at random (MCAR) and dropped from the study.

3.8.6 Statistical Techniques

The statistical approach for investigating the association between the outcome variables and the independent variables was to consider first the most powerful and robust methods of analysis. If a model was unable to meet the test assumptions, a less powerful statistical test, for which the assumptions could be reasonably met, was used.

Preliminary analyses were conducted with paired t-tests to determine magnitude of differences between the before and after group for each dependent variable. In analyses with a continuous dependent variable, hypotheses were then tested using ordinary least squares regressions. In analyses with a dichotomous dependent variable, hypotheses were tested using multiple logistic regression. Robust regression models were used if other attempts to normalize variable distribution failed.

As with any mathematical model, multiple regression techniques involve assumptions about the characteristics of, and relationships between the dependent and independent variables. Assumptions relevant to logistic regression are presented in Table 3.5 while those for multiple linear regression are presented in Table 3.6. Methods for detecting violations are presented as well. All statistical tests in this research were performed with an alpha level of 0.05 considered as statistically significant.

Analyses utilizing logistic regression are discussed first, followed by those using ordinary least square regression. The discussions do not necessarily follow the order the hypotheses were stated.

Table 3.5 Assumptions Relevant to Logistic Regression Models

<i>Assumption</i>	<i>Diagnostic Method</i>	<i>Correction</i>
Linearity in log-odds	No automatic plots since value of the dependent variable is either 0 or 1	
Normality	Not applicable since dependent variable is binary	
Outliers in Y (predicted probabilities)	Detected using residuals – graph leverage versus deviance residual	Examine data points with high leverage, large residuals
Independent residuals	Best method of detection is to plot residuals (Pearson or deviance) versus each of the X_i . Residuals should have a random pattern.	Report in discussion section
No multicollinearity	Best method of detection is to examine correlation matrix among the X_i .	Delete one of the X_i since essentially the same info

3.8.7 Association Between Guideline Use and Asthma Exacerbations

Logistic regression was used to investigate the relationship between asthma exacerbations and CPG use as expressed in H_0 : 4. The dependent variable was the presence or absence of an asthma exacerbation within the study period. The primary independent variable was the presence or absence of CPG use. Other independent variables included MTF size, MTF service type, gender, age, service type, TRICARE region, beneficiary category, care received in multiple facilities, presence or absence of lead agent MTF, presence of respiratory comorbidities, and interaction terms as described in section 3.8.4.

Since the dependent variable of this analysis was dichotomous (presence or absence of asthma exacerbations), a multiple logistic regression model was used.

There are several reasons for using logistical regression. First, from a mathematical perspective, it is flexible and easy to use. Second, from an explanatory and predictive perspective, it has the ability to estimate the magnitude of associations between variables, while simultaneously adjusting for other potentially confounding factors. More importantly, logistic regression lends itself to biologically meaningful interpretations – an important element in these analyses since they are intended to assist decision makers identify practical opportunities in which guidelines may be incorporated into asthma therapy.(199)

Table 3.6 Assumptions Relevant to Multilinear Regression Models

<i>Assumption</i>	<i>Diagnostic Method</i>	<i>Correction</i>
Linearity	Plot of the residuals versus each X_i ; residuals should have a random pattern	Transform either Y or X or both
Normality of continuous variables	1. Plot of the residuals versus each of the X_i 2. Histogram or normal probability plots of the residuals	Transform either Y or X or both
No outliers in X or Y	1. Outliers in X can be detected using the leverage 2. Outliers in Y can be detected using the studentized residual 3. Influence of outliers can be quantified using Cook's distance	1. Check for input or coding errors 2. Alternative approach: Fit line, examine residuals, remove observations that are outlying an influential, then refit regression line. (This approach can lead to incorrect inferences of data) 3. Describe outliers in results
Variance of Y does not depend on level of X	1. Plot of the residuals versus each of the X_i ; residuals should have a random pattern 2. Cook and Weisberg test for heteroscedasticity	1. Transformation 2. Weighted least squares; observations are weighted according to their relative importance or degree of variability
No measurement error in X	Often assessed subjectively	1. Describe data
Independent residuals	1. Often based on subject matter principles. 2. Plot of the residuals versus each of the X_i ; residuals should have a random pattern 3. Can use the Durbin-Watson statistic to test the hypothesis that serial correlation coefficient is 0	1. Longitudinal data analysis methods or time series analysis
No multi-collinearity	1. Examine correlation matrix among the X_i 2. Most computer programs have built-in checks	1. Delete one of the X_i since essentially the same information

Logistic regression is a statistical technique in which the outcome (dependent variable) is expressed as a function of predictor or explanatory (independent) variables. Specifically, the dependent variable is defined as the natural logarithm (ln) of the odds of the outcome, or the logit. If 'Y' is the probability of the outcome, then $Y/(1-Y)$ represents the "odds"

of developing the outcome, and the log odds of the outcome, or the logit, can be written as $\ln[Y/(1-Y)]$. The log odds of the outcome as the dependent variable can then be expressed as a simple linear function of the independent predictor or explanatory variables using equation 3.1:(123)

Equation 3.1:

$$\ln\left[\frac{Y}{1-Y}\right] = \alpha + \beta_1 X_1 + \dots + \beta_n X_n$$

This equation can be rewritten to represent the probability of disease as shown in equation 3.2:(123)

Equation 3.2:

$$Y = \frac{1}{1 + e^{-(\alpha + \beta_1 X_1 + \dots + \beta_n X_n)}}$$

The specific set of values for the intercept α and for β_1, \dots, β_n in logistic regression are calculated to represent those that provide the most likely estimate of the population from which the data arose. Since the logistic model for the probability of the outcome always results in values between zero and one, its use has important implications for the interpretation of the coefficients. The coefficients obtained through logistic regression by definition reflect the magnitude of increase or decrease in the log odds produced by one unit change in the values of the independent variable and thus indicate the effect of an

individual factor on the log odds of the outcome with all remaining variables held constant. The practical application is that these coefficients can be directly converted to an odds ratio that provides an estimate of the relative risk that is adjusted for confounding.(123) An estimation of the relative risk and the 95 percent confidence intervals around the relative risk can be calculated from Equations 3.3 and 3.4 respectively:(123)

Equation 3.3:

$$RR(x_i) = e^{\beta_i}$$

Equation 3.4:

$$95\%CI = e^{(\beta_i \pm 1.96E\beta_i)}$$

To examine the overall association between ‘asthma exacerbation’ and ‘guideline use’ a crude odds ratio was determined using Equation 3.5, in which ‘Y’ represented the presence or absence of an asthma exacerbation, and ‘cpg’ represented the presence or absence of MTF guideline use for delivering asthma care. This estimation was then refined by adding the influence of covariates to the model as expressed in Equation 3.6.

The association between individual covariates and asthma exacerbations was also determined using equation 3.6. This model provided estimates (ORs) of the magnitude of association between each covariate and risk of asthma exacerbation after adjusting for the

other covariates. The significance of each odds ratio in the analyses was determined by calculating 95 percent confidence intervals (CI). If the value of '1' was not included within the CI range, the OR was considered significant.

Equation 3.5: Unadjusted Model

$$\ln\left[\frac{Y}{1-Y}\right] = \alpha + \beta(cpg) + e$$

where: 'Y' = the probability of having an asthma exacerbation; 'cpg' = the presence or absence of guideline use; and 'e' = model error

Equation 3.6: Adjusted Model

$$\begin{aligned} \ln\left[\frac{Y}{1-Y}\right] = & \alpha + \beta_1(cpg) + \beta_2(F_cat) + \beta_3(F_Type) + \beta_4(L_type) + \\ & \beta_5(mult_F) + \beta_6(sex) + \beta_7(age_cat) + \beta_8(otmtreg) + \beta_9(f_bencat) + \\ & \beta_{10}(comd) + \beta_{11}(svc) + \beta_{12}(int1) + \beta_{13}(int2) + \beta_{14}(int3) + \beta_{15}(V) + e \end{aligned}$$

where: 'Y' = the probability of having an asthma exacerbation; V = the variable in the before period corresponding to the dependent variable, and 'e' = model error.

3.8.8 Hypotheses utilizing Multiple Linear Regression

Hypotheses H₀:1 to H₀:6 with the exception of H₀:4 were analyzed using linear regression techniques. The distinguishing characteristic of linear regression is that the outcome of interest is represented as a continuous variable. Permutations of linear regression used in these analyses include analysis of variance (ANOVA) in which all the independent

variables are categorical, and analysis of covariance (ANCOVA) in which the independent variables are a mixture of categorical and continuous.(200) Multiple linear regression is an extension of simple linear regression which describes the linear relationship between two variables. In simple linear regression, the relationship between the mean of the dependent variable 'Y' and an independent variable 'X' is expressed as equation 3.7:

Equation 3.7 Simple Linear Regression

$$Y = \alpha + \beta(X)$$

where: α is the linear regression intercept, and β is the slope of the line representing the association between X and Y.

Another way of describing β is that it is the estimated mean change in the expected value of the dependent variable for each unit change of the independent variable. Multiple linear regression involves expanding equation 3.7 to include multiple independent variables as shown in equation 3.8:

Equation 3.8: General Multiple Linear Regression Model

$$Y = \alpha + \beta_1 X_1 + \beta_2 X_2 + \dots \beta_n X_n$$

where: n = the number of independent variables

$X_1 \dots X_n$ = the particular set of values for the independent variables, and

$\beta_1 \dots \beta_n$ = the respective coefficients for each of the independent variables.

As with the simple linear regression model, the coefficients of specific independent variables within a multiple linear regression model can be interpreted as the magnitude of change that occurs in the dependent variable for every unit change in the independent variable of interest. This is after accounting for the effects of the other independent variables in the model.(123) The null hypothesis for this model is that the partial-regression coefficients are simultaneously equal to zero ($H_0: \beta_1 = \beta_2 = \dots \beta_k = 0$). The alternate hypothesis would be that at least one of the partial-regression coefficients is not equal to zero (H_1 : At least one $\beta_j \neq 0$). To determine the proportion of variance in the dependent variable that is explained by the set of independent variables in the model the coefficient of determination (R^2) is used. R^2 , the square of the Pearson correlation coefficient r , has a range between zero and one. If $R^2 = 1$, the relationship between the dependent and independent variables is totally linear (all data points in the sample fall directly on the least-squares line). If $R^2 = 0$, there is no linear relationship between the dependent and independent variables. To determine the overall significance of the model, a p-value is reported based on the F -test (regression mean of squares/residual mean of squares). To determine the significance of the relationship of each independent variable to the dependent variable, individual p-values (based on the t -test) are reported.

3.8.9 Association Between Guideline Use and Direct costs of Asthma (H_0 : 1)

The purpose of this analysis was to investigate the relationship between CPG use and the direct cost of providing asthma care. The continuous dependent variable was the direct cost associated with providing asthma therapy within the study timeframe, and the

primary independent variable was the presence or absence of CPG use. As with the previous analysis, independent variables in the model were categorical and included MTF size, MTF service type, gender, age, service type, TRICARE region, beneficiary category, care received in multiple facilities, presence or absence of a lead agent MTF, presence of respiratory comorbidities, and interaction terms as described in section 3.8.4.

3.8.10 Association Between Guideline Use and Health Care Encounters Related to Asthma (H_0 : 2)

The purpose of the second analysis was to investigate the relationship between CPG use and total number of asthma related health encounters. The continuous dependent variable was the number of health encounters experienced within the study timeframe; the primary independent variable was the presence or absence of CPG use. Total number of encounters included inpatient visits, outpatient visits, and number of prescriptions dispensed. As with the analysis described for H_0 :1 other independent variables in the model included MTF size, MTF service type, gender, age, service type, TRICARE region, beneficiary category, care received in multiple facilities, presence or absence of a lead agent MTF, presence of respiratory comorbidities, and interaction terms as described in section 3.8.4. Since the dependent variable of this analysis was continuous, multiple linear techniques were used.

3.8.11 Association Between Guideline Use and Health Care Visits Related to Asthma (H_0 : 3)

The purpose of this analysis was to investigate the relationship between CPG use and total number of asthma related visits as defined by inpatient and outpatient visits only

(prescription encounters excluded). The continuous dependent variable was the number of health care visits experienced within the study timeframe and the primary independent variable was the presence or absence of CPG use. As with the analyses already described, the independent variables in the model included MTF size, MTF service type, gender, age, service type, TRICARE region, beneficiary category, care received in multiple facilities, presence or absence of a lead agent MTF, presence of respiratory comorbidities, and interaction terms as described in section 3.8.4. Since the dependent variable of this analysis was continuous, multiple linear techniques were used.

3.8.12 Association Between Guideline Use and the Number of Prescriptions Dispensed for Asthma Care. (H_0 : 5)

The purpose of this analysis was to investigate the relationship between CPG use and total number of prescriptions dispensed for the treatment of asthma. The continuous dependent variable was the total number of prescriptions dispensed for the treatment of asthma within the study timeframe and the primary independent variable was the presence or absence of CPG use. As with the previous analyses, the independent variables in the model included MTF size, MTF service type, gender, age, service type, TRICARE region, beneficiary category, care received in multiple facilities, presence or absence of a lead agent MTF, presence of respiratory comorbidities, and interaction terms as described in section 3.8.4. Since the dependent variable of this analysis was continuous, multiple linear techniques were used.

3.8.13 Association Between Guideline Use and Length of Hospital Stay for a Primary Diagnosis of Asthma (H_0 : 6)

The same statistical tests and assumptions used in the previous analysis were used in this analysis. The dependent variable in the this analysis was the length of hospitalization (in days) and the primary independent variable was CPG use. As with the previous analyses, other independent variables were categorical and included MTF size, MTF service type, gender, age, rank of sponsor, ethnicity, TRICARE region, duty status, respiratory comorbidities, and the interaction terms described in section 3.8.4.

3.8.14 Association between guideline use and frequency of long-term controller medications. (H_0 : 7)

This analysis examined the relationship between the number of long-term controller medication (LTC) prescriptions dispensed, and exposure to the CPG-use process. Specific agents included in these analyses are listed in table 3.7.

Table 3.7: Long-term controller medications included in analyses

<i>Inhaled Corticosteroids</i>	
	Beclomethasone dipropionate 42 & 84 mcg/puff
	Budesonide Turbohaler 200mcg/dose
	Fluisolide 250mcg/puff
	Fluticasone MDI 44, 110, 220 mcg/puff
	Fluticasone DPI 50, 100 mcg/puff
	Triamcinolone acetone 100mcg/puff
<i>Mast-Cell Stabilizer</i>	
	Cromolyn sodium 800mcg/dose

One of the methods used to perform this analysis was the chi-square test. The general format of this test is equation 3:10. The assumptions of the chi-square statistic are:(201).

- all data is the function of a frequency count;
- the expected value in any cell should be no less than five;
- the sum of the expected frequencies must equal the sum of the observed frequencies; and
- each score must have a value independent of all other scores.

Equation 3.10: General formula for chi-square.(202)

$$\chi^2 = \sum_{i=1}^{rc} \frac{(O_i - E_i)^2}{E_i}$$

where rc is the number of cells in the table, O represents observed cell frequencies, and E represents expected frequencies.

The contingency table used to conduct the chi-square analysis is shown below in Table 3.8. Subjects considered positive (Yes) for controller medication use were those for whom at least one prescription for either a inhaled corticosteroid or mast cell stabilizer was abstracted from the USPD drug file over the course of the study period.

Table 3.8: Chi-Square Contingency Table: Guideline Use and the Use of Controller Medications

	Long-term controller use		Total
	Yes	No	
CPG use process			
Yes	a	b	a + b
No	c	d	c + d
Total	a + c	b + d	n

To determine if there was a difference between groups in the proportion of subjects with a long-term controller medication in the period after CPG implementation, a two-sample test of proportions was used. The null hypothesis for this test is that the success probabilities in each population are the same ($H_0: p_1 = p_2$).⁽²⁰³⁾

Because of the paired nature of the data in these analyses the McNemar test was also used. The null hypothesis is that the paired proportions are equal between groups, and the alternative hypothesis is that the paired proportions are not equal.⁽²⁰⁴⁾ This test uses only the number of discordant pairs in the analyses as the concordant pairs provide no information for testing the null hypotheses.⁽²⁰²⁾ The general equation for the McNemar's chi-square test is presented as equation 3.11.⁽²⁰⁵⁾

Equation 3:11 McNemar's Chi-Square test for paired observations

$$\chi^2 = \frac{[(r - s) - 1]^2}{(r + s)}$$

where r and s represent the number of pairs (discordant) in which a long-term controller medication was dispensed in either the period after CPG implementation (r) or the period before (s), but not both. The other pairs (concordant) were matched such that long-term controllers were dispensed in either both periods, or not in either period.

3.9 Assumptions

Based upon the database and variables used in this research, the following assumptions were made.

SIDR/SADR and USPD data were representative of the health care issues of asthma patients within the DoD population: It was assumed that all asthma related health care encounters and resources used, were captured by the databases used in this study. For the most part, this is probably a valid assumption for two reasons. First there are financial incentives for eligible beneficiaries to use the MHS for health care rather than other sources, and second, active duty members are directed by regulation to obtain their care through channels provided by the MHS. A situation in which this assumption might not be valid is in the case of an acute asthma exacerbation. In this case it would be expected that the subject would seek treatment at the nearest treatment facility which may or may not be a military MTF.

Within the study cohort, asthma care was administered according to the DOD Clinical Practice Guidelines: It was assumed that after guideline implementation, physicians at participating MTFs had fully incorporated the guideline recommendations into their treatment plans for asthma. This is likely to be a valid assumption given a planned strategy within the DoD for implementation and institutionalization of asthma guidelines, and the accountability provided by follow-up metrics.

3.10 Limitations

Limitations to this research are discussed below.

The first limitation was the use of ICD-9 coding for selection of asthmatics and comorbid diseases. ICD-9 coding errors can occur for a number of reasons. These include misclassification of disease, miscoding, incorrect sequencing decisions, variability in coding (between MTFs, physicians, and offices), and clerical mistakes. Additionally, although ICD-9 codes can provide a diagnosis, they are unable to differentiate between treatment methods or issues of severity.

Another limitation was the use of EBC codes for capturing direct costs of procedures. Similarly to the limitations associated with the use of ICD-9 codes, miscoding and clerical errors can occur when EBC codes are used. Also, physicians may not accurately

assign EBC codes or assign them at all. Additionally, EBC codes reflect relative, and not actual prices.

There are several issues associated with the validity of the prescription database. These include: 1) member ID errors (duplicate information, errors in gender, date of birth, etc), 2) drug code errors (wrong drug code used, different units of use between MTFs), and, 3) prescriber ID problems (no uniform number for each prescriber across all claims, fictional prescriber numbers). Another potential limitation was the multiple sources available for subjects for obtaining prescriptions. Although it was assumed that subjects who received their asthma care from military MTFs also received their prescriptions from MTF pharmacies, this assumption could be invalid due to the increasing popularity of the retail pharmacy network and national mail order pharmacy options available to military beneficiaries.

As mentioned earlier, this study did not capture asthma exacerbations treated outside of the MHS. This could be a major limitation as many MHS beneficiaries live in communities outside the military post or base that operate the MTF. In these instances, a patient seeking care for an asthma exacerbation would probably seek care from the community based treatment facility closest to where the exacerbation occurred.

Finally, the population under investigation in this study consists only of DoD beneficiaries. Furthermore, only subjects treated in both the before and after periods of

CPG exposure were included in the study. Therefore the results of this study are only generalizable to this group of subjects

3.11 Summary

This chapter provided the methodological framework for evaluating the relationships between asthma CPG use in the DoD relative to: (1) direct cost of asthma therapy; (2) frequency of asthma related health care encounters including prescriptions; (3) frequency of an inpatient or ambulatory health care visit (excluding prescriptions); (4) risk of an asthma exacerbation; (5) the number of prescriptions dispensed for asthma; (6) days of hospitalization associated with a primary diagnosis of asthma; and (7) the association between guideline use and the use of long-term controller medications. The general limitations of an observational before-after study design have been recognized along with limitations inherent in using claims databases for outcomes research. In spite of these limitations however, the study design and database used in this research provides the DoD with an opportunity for obtaining reliable estimates of the clinical and economic benefits of asthma guidelines without the cost and ethical problems associated with a randomized clinical trial.

Chapter 4: Results

4.1 Introduction

This chapter presents the results of analyses examining the effect of CPGs on clinical and economic outcomes of subjects treated for asthma within the United States DoD. The results presented in this chapter include: (1) descriptive statistics of the study population, (2) the association, after adjusting for confounders, between clinical and economic outcomes of asthma and CPG use, and (3) factors influencing clinical and economic outcomes of asthma therapy within the DoD based on statistically significant independent variables.

4.2 Descriptive Statistics

The query of the PEC databases identified 216,883 unique subjects within 690 military health service facilities that had utilized outpatient services for asthma therapy. This included 4,136 subjects that had been hospitalized for asthma, and 114,398 subjects that had received at least one asthma-related prescription medication between 1 January 2000 and 31 December 2001. After merging by subject ID numbers, the total number of individuals was 218,166. The mean number of total health care encounters per subject for the total time period was 6.61 ± 9.34 . Table 4.1 presents the total number of health care encounters and subjects during the study period for each type of encounter.

Table 4.1: Composition of entire data set

<i>Type of health care encounter</i>	<i>Health care encounters</i>	<i>Unique subjects</i>
Asthma-related hospitalizations	4,705	4,136
Asthma-related outpatient visits	571,673	216,883
Asthma-related prescriptions	864,356	114,356
Totals	1,440,734	218,166

Table 4.2 presents subject distributions within the entire data set based on data characteristics and military service type of MTF.

Table 4.2: Entire Data Set - Distribution of subjects based upon MTF service type

<i>Variable</i>	<i>Categories</i>	<i>Army</i>	<i>Navy</i>	<i>Air Force</i>	<i>Other</i>	<i>X²</i>	<i>p-value</i>
Age	5 -12 yrs	28070	22686	23349	253		
	13-18 yrs	12570	9507	10458	212		
	19-40 yrs	45268	31608	33053	1132	0234.39	< 0.001
Gender	Male	40297	28986	31608	466		
	Female	45611	34815	35252	1131	50.46	< 0.001
Affiliation	Army	73908	3012	6040	656		
	Navy	5532	57639	5103	670		
	Air Force	5157	1782	54836	212		
	Other	1311	1368	881	59	208381	< 0.001
Beneficiary Category	Dependent of active duty	52330	42814	42558	1049		
	Retired	583	478	494	16		
	Dependent of retired	9209	6547	8959	247		
	Active Duty	23786	13962	14849	285	1245.16	<0.001
Size of Facility	0 to 250	3248	3458	427	9		
	251 to 500	3756	3625	981	310		
	501 to 1000	6549	2346	4507	6		
	1001 to 2000	10183	14150	14180	69		
	2001 to 3000	7630	7605	14048	32		
	> 3000	54542	32617	32717	1171	13762	< 0.001
Lead Agent Facility	Lead Agent	9444	8430	9733	459		
	Other MTF	76464	55371	57127	1138	447.03	< 0.001
Multiple Facilities	Multiple MTFs	11226	6721	5179	45		
	Single MTF	74682	57080	61681	1552	1118.22	< 0.001
Comorbidity Status	Comorbidity	58517	45046	48832	404		
	No Comorbidity	27391	18755	18028	1193	438.95	< 0.001
TRICARE Region	Region 1	11355	6609	4341	146		
	Region 2	8883	13637	3018	455		
	Region 3	10408	7571	4572	122		
	Region 4	1821	2371	6306	70		
	Region 5	6970	2943	3986	119		
	Region 6	13855	1047	12165	162		
	Region 7/8	12464	103	17007	117		
	Region 9	600	15968	1605	150		
	Region 10	160	1132	3021	16		
	Region 11	4273	3947	955	53		
	Non-Conus*	15119	8473	9884	170	76013	< 0.001

* Non-conus refers to TRICARE regions outside of the continental United States

As seen in Table 4.3, the mean age for subjects treated at Air Force facilities was significantly higher than those seen at Army facilities, which in turn was somewhat higher than those treated at Navy facilities. In all three military services, a significantly greater proportion of subjects treated for asthma were females as opposed to males. This ranged from a high of 54.5 percent females in the Navy to a low of 52.7 percent in the Air Force. With respect to gender, there was a significant difference between military services.

Table 4.3: Entire data set: age and gender across military service types

<i>Demographic Characteristics</i>	<i>Army (n = 83616)</i>	<i>Navy (n = 68944)</i>	<i>Air Force (n = 61987)</i>	<i>Other (n = 3619)</i>	<i>Statistic</i>	<i>p-value</i>
Mean age (SD)	20.08 (10.68)	19.70 (10.99)	20.41 (11.46)	22.66 (9.15)	$\chi^2 = 3006$ df = 105	0.0001
Gender (%)						
Males	40297 (46.91%)	28989 (45.43%)	31608 (47.27%)	466 (29.18%)	$\chi^2 = 243$ df = 3	0.0001
Females	45611 (53.09%)	34815 (54.57%)	35252 (52.73%)	1131 (70.82%)		

As seen in Table 4.4, mean total costs associated with asthma therapy ranged from a high of \$684.65 per patient in the Navy to a low of \$611.47 in the Air Force. For all three services, inpatient/outpatient costs comprised the largest segment of total asthma treatment costs. These ranged from a high of \$607.65 per treated subject in the Navy to a low of \$527.89 for subjects treated in an Air Force facility.

Table 4.4: Entire data set: comparison of cost, health care encounter, and exacerbation variables across military service type

<i>Outcome variable</i>	<i>Army</i>	<i>Navy</i>	<i>Air Force</i>	<i>f-statistic (p-value)</i>
Mean total cost (SD)	\$651.09 (\$3257.57)	\$684.65 (\$8570.58)	\$611.47 (\$2805.88)	2.91 (0.054)
Mean prescription cost (SD)	\$80.66 (\$422.56)	\$76.99 (\$298.75)	\$83.57 (\$459.06)	4.49 (0.01)
Mean inpatient/outpatient cost (SD)	\$570.42 (\$3193.05)	\$607.65 (\$8549.78)	\$527.89 (\$2738.99)	3.50 (0.03)
Mean health care encounters including Rx's (SD)	6.67 (9.43)	6.36 (9.06)	6.84 (9.58)	43.91 (<0.0001)
Mean inpatient/outpatient visits (SD)	2.74 (3.57)	2.55 (3.49)	2.66 (3.21)	55.25 (<0.0001)
Mean prescriptions dispensed (SD)	3.94 (7.27)	3.81 (6.98)	4.16 (7.69)	40.05 (<0.0001)
Mean exacerbations (SD)	0.11 (0.37)	0.11 (0.49)	0.07 (0.33)	213.62 (<0.0001)
Mean inpatient beddays (SD)	0.07 (0.99)	0.07 (0.72)	0.04 (0.58)	19.73 (<0.0001)

4.2.1 Comparison of Before/After and One Period Subjects

Of the 216,883 subjects in the entire data set, 71,890 had at least one observation both before and after the implementation of asthma clinical practice guidelines, while 146,276 subjects had observations in only the before or after group. As seen in Table 4.5, the composition of the those with encounters in one or both periods was significantly different in terms of both age and gender. The before/after group was comprised of significantly more female subjects than the unmatched group ($p < 0.001$), and on average, the subjects in the before/after group were two years younger than those in the one period group ($p < 0.0001$).

In addition to age and gender, cost and disease variables also differed between the matched and unmatched groups. This was not entirely unexpected, however, as by definition, those in the before/after group were required to have at least two observations since they appeared both before and after CPG implementation, while those in the one period group only appeared in the before or after group. Although there were no variables in the original database to adjust for severity, repeated health care visits, known to be the case for those in the matched group, could be indicative of a more severe disease status. A difference in disease severity, not captured in this data set, could offer an additional explanation for the differences observed between the two groups as observed in Table 4.5.

Table 4.5: Demographic and utilization comparison for before/after and one period subjects

<i>Demographic Characteristic</i>	<i>Matched Subjects (n = 71890)</i>	<i>Unmatched Subjects (n = 146276)</i>	<i>Statistic</i>	<i>p-value</i>
Mean subject age (SD)	18.72 (11.18)	20.77 (10.89)	t = - 40.95	< 0.0001
Gender				
Male (%)	33083 (46.02 %)	68274 (46.67 %)	$\chi^2 = 8.33$ (df = 1)	< 0.001
Female (%)	38807 (53.98 %)	78002 (53.33 %)		
Mean total cost (SD)	\$1177.15 (\$5655.96)	\$392.19 (\$5313.33)	t = 31.74	< 0.0001
Mean cost of inpatient/outpatient visits (SD)	\$973.99 (\$5582.94)	\$372.09 (\$5307.20)	t = 24.48	< 0.0001
Mean number of health care encounters (SD)	13.79 (12.62)	3.08 (3.79)	t = 306.33	< 0.0001
Mean number of prescriptions dispensed (SD)	9.49 (10.11)	1.24 (2.65)	t = 292.33	< 0.0001
Mean number of inpatient/outpatient visits (SD)	4.30 (4.90)	1.84 (1.94)	t = 167.19	< 0.0001
Mean number of asthma exacerbations (SD)	0.11 (0.56)	0.09 (0.29)	t = 10.98	< 0.0001
Mean number of inpatient beddays (SD)	0.10 (1.08)	0.04 (0.64)	t = 16.22	< 0.0001

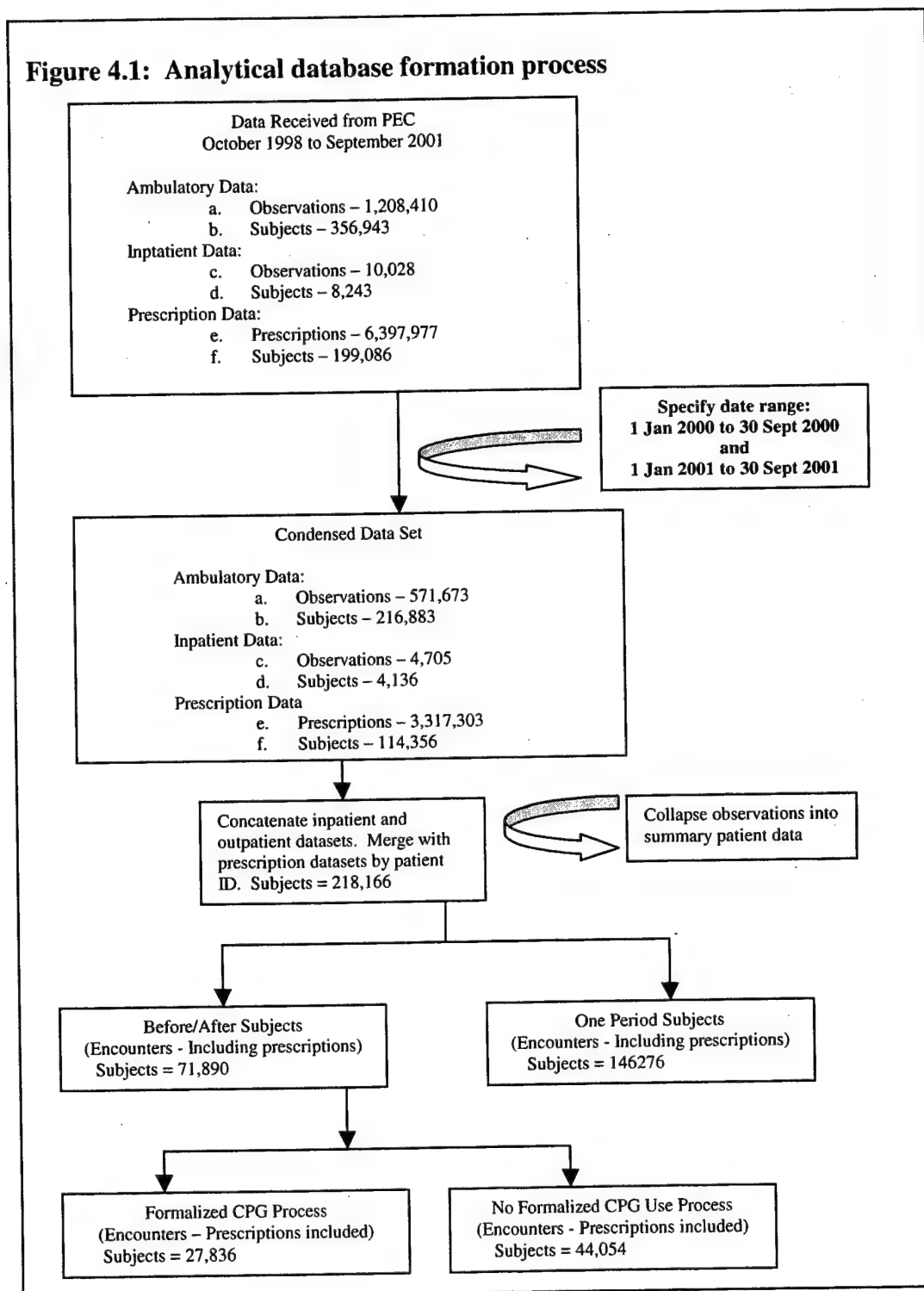
4.2.2 Before/After data set

As discussed in the methods section, these analyses were conducted using subjects that were observed to have health care observations in both the before and after time periods. Of the 71,890 subjects that met this criterion, 26,945 (37%) received health care through an Army MTF, 22,182 (31%) through a Navy MTF, 21,754 (30%) through an Air Force MTF, and 1009 (2%) in which the MTF type was not specified. The distribution of subjects by military service type is shown in Table 4.6. The complete data formation process for use in these analyses is illustrated in Figure 4.1.

Table 4.6: Before/After data set: Comparison of service type demographics by age, gender, affiliation, beneficiary category, facility size, lead agent, multiple facilities, comorbidity status, and TRICARE region

<i>Variable</i>	<i>Categories</i>	<i>Army</i>	<i>Navy</i>	<i>Air Force</i>	<i>Other</i>	<i>X²</i>	<i>p-value</i>
<i>Age</i>	5 -12 yrs	11011	8756	9833	45		
	13-18 yrs	4076	3087	3859	32		
	19-40 yrs	12749	8661	9670	111	118.91	< 0.0014
<i>Gender</i>	Male	12932	9086	11006	59		
	Female	14904	11418	12356	129	36653.00	< 0.001
<i>Affiliation</i>	Army	23656	1046	2160	83		
	Navy	1900	18406	1798	78		
	Air Force	1943	631	19155	25		
	Other	337	421	249	2	90515	< 0.001
<i>Beneficiary Category</i>	Dependent of active Duty	18415	14982	16188	130		
	Retired	205	160	157	2		
	Dependent of retired	3483	2382	3539	36		
	Active Duty	5733	2980	3478	20	546.27	< 0.001
<i>Size of Facility</i>	0 to 250	825	867	152	0		
	251 to 500	1110	872	324	62		
	501 to 1000	1699	681	1417	1		
	1001 to 2000	2691	4178	4959	6		
	2001 to 3000	2644	2269	4648	4		
	> 3000	18867	11637	11862	115	4224.70	< 0.001
<i>Lead Agent Facility</i>	Lead Agent	3393	3522	3710	48		
	Other MTF	24443	16982	19652	140	263.69	< 0.001
<i>Multiple Facilities</i>	Multiple MTFs	6202	3887	3490	8		
	Single MTF	21634	16617	19872	180	445.97	< 0.001
<i>Comorbidity Status</i>	Comorbidity	58517	45287	48832	4		
	No Comorbidity	27391	18824	18028	0	439.57	< 0.001
<i>TRICARE Region</i>	Region 1	4019	2200	1582	14		
	Region 2	2918	5024	975	63		
	Region 3	2970	2357	1557	12		
	Region 4	595	693	2173	10		
	Region 5	1869	554	1457	19		
	Region 6	4758	306	4265	10		
	Region 7/8	3907	40	5978	15		
	Region 9	200	5040	531	19		
	Region 10	46	377	1111	2		
	Region 11	1496	1318	304	7		
	Non-Conus	5058	2595	3429	15	26742.64	< 0.001

Figure 4.1: Analytical database formation process



As described in the methods section, for the purposes of these analyses the use of a formalized CPG process was synonymous with receiving asthma care at an Army medical treatment facility. Care received at a medical treatment facility other than Army was considered to be synonymous with no formal asthma CPG use. As illustrated in Figure 4.1, there were 27,836 subjects in the formalized CPG use group and 44,054 subjects in the group not using a formalized CPG use process. Variable distributions for both groups are illustrated in Table 4.7.

Table 4.7: Before/After data set: Comparison of CPG-use demographics by age, gender, affiliation, beneficiary category, facility size, lead agent, multiple facilities, comorbidity status, and TRICARE region

<i>Variable</i>	<i>Category</i>	<i>Formalized CPG Use</i>	<i>No Formal CPG Use Process</i>	<i>f or t statistic</i>	<i>p-value</i>
<i>Age</i>	5 -12 yrs	11011	18634		
	13-18 yrs	4076	6978		
	19-40 yrs	12749	18442	107.94	< 0.001
<i>Gender</i>	Male	12932	20151		
	Female	14904	23903	3.52	0.061
<i>Affiliation</i>	Army	23656	3289		
	Navy	1900	20282		
	Air Force	1943	19811		
	Other	337	672	43951.86	< 0.001
<i>Beneficiary Category</i>	Dependent of active duty	18415	31300		
	Retired	205	319		
	Retired dependent	3483	5957		
	Active duty	5733	6478	420.85	< 0.001
<i>Size of Facility</i>	0 to 250	825	1019		
	251 to 500	1110	1258		
	501 to 1000	1699	2099		
	1001 to 2000	2691	9143		
	2001 to 3000	2644	6921		
	> 3000	18867	23614	2500.97	< 0.001
<i>Lead Agent Facility</i>	Lead agent	3393	7280		
	Other MTF	24443	36774	253.67	< 0.001
<i>Multiple Facilities</i>	Multiple MTFs	6202	7385		
	Single MTF	21634	36669	103.00	< 0.001
<i>Comorbidity Status</i>	Comorbidity	15594	26048		
	No comorbidity	12242	18006	67.54	< 0.001
<i>TRICARE Region</i>	Region 1	4019	3796		
	Region 2	2918	6062		
	Region 3	2970	3926		
	Region 4	595	2876		
	Region 5	1869	2030		
	Region 6	4758	4581		
	Region 7/8	3907	6033		
	Region 9	200	5590		
	Region 10	46	1490		
	Region 11	1496	1629		
	Non-Conus*	5058	6039	6335.34	< 0.001

* Non-conus refers to TRICARE regions outside of the continental United States

4.3 Bivariate analyses

Preliminary analyses, using paired t-tests, were conducted to compare the means of each of the dependent variables in the periods before and after asthma CPG implementation. The analyses were conducted for both the CPG use group and the no-CPG use group. The effects of variables other than the dependent variables being compared, were not controlled for in the preliminary analyses. The means of the dependent variables for both the CPG group and the control group (no-CPG use) are presented in Table 4.8.

Table 4.8: Total cost and utilization of CPG and control groups

<i>Comparator Groups</i>	<i>CPG Group</i>		<i>Control Group</i>	
Dependent Variable	Mean values in period before CPG implementation (Standard deviation))	Mean values in period after CPG implementation (Standard deviation))	Mean values in period before CPG implementation (Standard deviation))	Mean values in period after CPG implementation (Standard deviation))
Total cost	\$556.21(\$3987.68)	\$412.93(\$2311.73)	\$545.17(\$3616.76)	\$431.88 (\$3430.64)
Prescriptions Dispensed	4.76(5.77)	4.70 (5.58)	4.80(5.65)	4.69(5.53)
Health Care Encounters	7.30(7.66)	6.72(7.19)	7.11(7.35)	6.53(6.81)
Health Care Visits	2.54(3.45)	2.01(3.26)	2.31(3.03)	1.83(2.77)
Beddays	0.071(1.08)	0.04(0.54)	0.06(0.66)	0.04(0.55)
Exacerbations	0.097(0.361)	0.02(0.18)	0.08(0.53)	0.02(0.22)

Changes in the mean values of the dependent variables between the period before, and the period after CPG exposure, are as follows: In the CPG group, total cost per subject decreased by \$143.282 ($p < 0.001$), total health care encounters decreased by 0.58 encounters ($p < 0.001$), health care visits decreased by 0.52 visits ($p < 0.0001$), total inpatient beddays decreased by 0.03 days per subject ($p < 0.001$), and number of

exacerbations experienced per subject decreased by 0.07 per subject ($p < 0.001$). No significant change occurred in the number of prescriptions dispensed.

In subjects treated at non-CPG facilities, total costs per subject during the same time period decreased by \$113.28 per subject ($p < 0.001$). In regards to the other dependent variables, total health care encounters decreased by 0.57 encounters ($p < 0.001$), health care visits decreased by 0.47 visits ($p < 0.001$), total inpatient beddays decreased by 0.02 days per subject ($p < 0.001$), and number of exacerbations experienced per subject decreased by 0.05 per subject ($p < 0.001$). In this group, a significant decrease of 0.10 prescriptions per subject was observed ($p < 0.001$).

There were no significant differences, except in the number of exacerbations, between the mean decrease (before and after CPG exposure) of the dependent variables (Table 4.9). This suggests that although significant changes in the means of the dependent variables occurred between the two time periods, the changes occurred similarly between the CPG and control groups, with the exception of number of exacerbations. In this case, the decrease in the number of exacerbations between periods was significantly different between groups ($p < 0.0001$).

Table 4.9: Comparison of change in cost and utilization between CPG and control groups

<i>Dependent Variable</i>	<i>CPG Group Mean change in after versus before period (standard deviation)</i>	<i>Control Group Mean change in after versus before period (standard deviation)</i>	<i>t-value</i>	<i>p-value</i>
Total Cost	- \$143.28 (\$4286.97)	- \$113.283 (\$3751.28)	0.99	0.32
Prescriptions Dispensed	- 0.0572 (4.9383)	- 0.1044 (4.7915)	- 1.27	0.17
Health Care Encounters	- 0.5805 (7.3514)	- 0.5748 (6.8280)	0.11	0.91
Health Care Visits	- 0.5233 (4.0507)	- 0.4704 ((3.5174)	1.84	0.06
Beddays	- 0.0336 (1.1313)	- 0.0212 (0.7503)	1.74	0.08
Exacerbations	- 0.0716 (0.3837)	- 0.0544 (0.5236)	4.70	< 0.0001

4.4 Hypotheses tests

The results of the hypotheses tests concerning the effects of the CPG use process on each of the dependent variables are presented in this section. As previously stated, the alpha level of significance was 0.05 for all hypotheses tests. This research was conducted using a two-tailed probability distribution because *a priori* the direction of the effect was unknown.

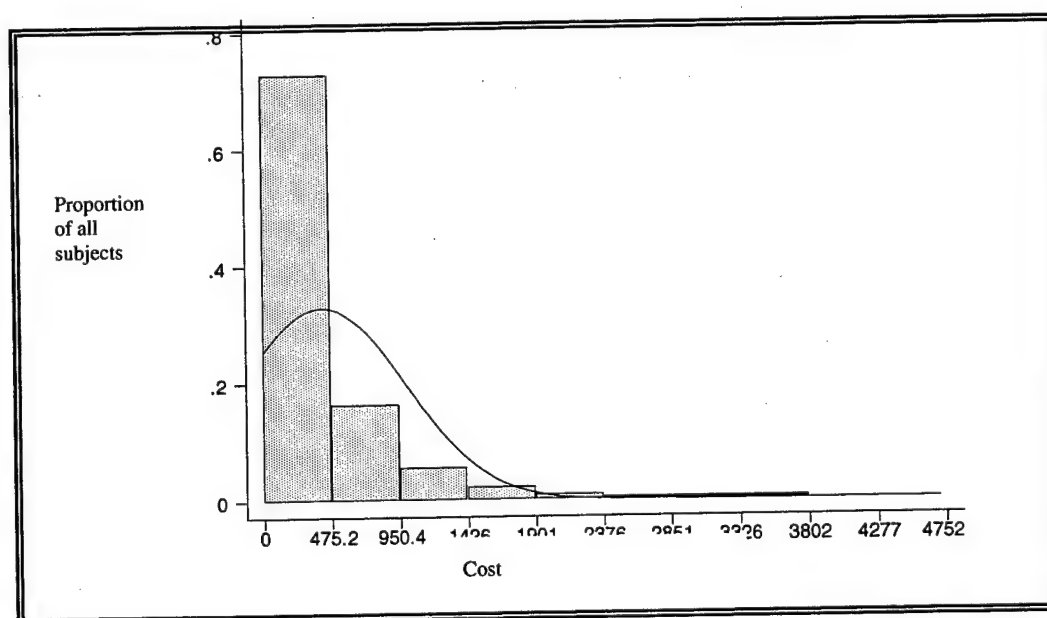
4.4.1 Total Costs

Ho: 1: There is no difference in the direct costs associated with asthma therapy between individuals treated before, and individuals treated after the implementation of the CPG-use process.

For all patients, total asthma costs in the period after asthma CPG implementation ranged from a low of \$0 to a high of \$499,576 with a mean of \$538 ± \$3103. For the period before CPG implementation, the range of the cost data was between \$0 and \$555,112

with a mean of $\$638 \pm \3798 . For the entire period, the maximum cost was $\$696,992$ with a mean of $\$1,177 \pm \$5,655$. Consistent with findings of other health care utilization research, a large number of observations were clustered at the lower end of the cost distribution, close to the mean.(206) There were however, a number of extreme observations that resulted in a non-normal distribution with a tail skewed heavily to the right as shown in Figure 4.2 (Costs truncated at 99th percentile for display purposes).

Figure 4.2: Distribution of total cost after asthma CPG implementation



According to Diehr and colleagues, using untransformed cost as a dependent variable in an OLS model is an appropriate method to predict future costs.(206) Despite the skewed distribution that generally occurs with utilization data, Diehr et. al. argue that procedures designed to normalize data, such as log-transformation, do not always result in a better prediction capability.(206)

The strategy for this analysis was to start with an OLS model using untransformed cost data and then proceed to transformed, robust, and logistic models, as required, to best meet model assumptions. Results would then be compared for consistency across different iterations of the model.

The initial model used for this analysis was a linear regression model. The model contained 12 independent variables. These included: CPG use; total costs before CPG implementation; gender; the presence of comorbid conditions; TRICARE region; the presence of multiple facilities for receiving care; a facility size variable; beneficiary category; age category; a variable indicating care received at a lead agent facility; and variables indicating the total number of prescriptions and inpatient/outpatient encounters during the study period. Variables dropped because of high correlation (> 0.3) with the CPG included the military service type of the subject and service affiliation of the medical treatment facility.

The overall model was significant with $p < 0.0001$. The model resulted in an overall R^2 of 0.1158, and an adjusted R^2 of 0.1155. This is consistent with the work of Newhouse and associates who state that the maximum R^2 for models predicting total cost are unlikely to be higher than about 15 percent.(207) According to Diehr, the low value of R^2 in total cost models is indicative of the difficulty of predicting costs of an individual as compared to making predictions regarding groups of individuals or populations.(206)

The use of a formalized CPG use process in delivering asthma therapy was found to have a significant effect in lowering total asthma therapy costs. After adjusting for the other variables in the model, the formal CPG use process decreased cost of asthma therapy by just over \$55 ($p = 0.021$). As shown in Table 4.10, the model also suggests significant regional cost differences in treating asthma subjects. Compared to TRICARE Region one (northeast), treatment costs were significantly lower in six of the TRICARE regions, with region eleven (northwest) having the lowest treatment costs per subject followed by region ten (golden gate). Areas in which cost was not significantly different from the northeast region include regions two (mid-atlantic), four (gulfsouth), five (heartland), and 12 (non-conus). It is also noteworthy to mention that total asthma costs were found to be \$123 ($p < 0.0001$) higher for subjects treated at lead agent facilities as compared to subjects treated at other MTFs. This should not be unexpected however, as lead agent facilities tend to be used as referral centers for other treatment facilities not as well equipped or staffed. Cost of asthma therapy also fluctuated according to facility size. Total costs for subjects treated in facilities associated with more than 3000 annual observations was \$262 more than for subjects treated in facilities with 250 or fewer observations ($p < 0.0001$). Again, because larger facilities are usually better equipped with staff and resources, it would not be unusual that they act as referral centers for more severe asthma cases, which would drive up costs. As would be expected, total treatment costs were higher for subjects who received care at more than one facility compared to those who received all their care at one facility. On average, costs increased by \$207 ($p <$

0.0001) for those receiving care at multiple facilities. Total costs for treating subjects in the thirteen to eighteen year age category was significantly less compared to those between in the five to 12 year old category ($p = 0.006$). There were no significant differences in the total cost of asthma therapy based on subject gender, comorbidity status, or beneficiary status. Interactions between age and gender and age and comorbidity were also tested in the model but found not to be significant and therefore, dropped.

Three different OLS models were used to evaluate the effect of asthma severity on the cost of treating asthma. The severity index of the first model was a dichotomous variable based on the number of health care visits experienced in the before-period, with three or more (cut point = 78th percentile) visits considered severe. The severity index for the second model was based on the presence or absence of an exacerbation(s) in the before period. The last severity index was based on the extent of β -agonist inhaler use in the pre-interventive period, with more use being indicative of greater severity. The addition of the first severity variable in the model had very little effect on total cost. The cost coefficient remained significant ($p = 0.021$) and increased from $-\$55.65$ to $-\$55.66$. The increase in cost associated with the severity variable was $\$6.90$, however, this was not significant ($p = 0.77$). When exacerbations were used as the severity index, the CPG coefficient remained significant and increased to $-\$59.47$. The cost associated with this measure of severity was $\$444.40$ ($p < 0.001$). When β -agonists were used as an indicator

of severity the cost savings associated with asthma therapy increased only slightly (-\$56.73, $p = 0.018$). The coefficients for these models are presented in Appendix F.

Table 4.10: OLS untransformed total cost model predicting total costs in after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-55.65337	24.07555	-2.310	0.021	-102.8414	-8.465358
Total cost before	0.272813	0.0028718	95.000	< 0.001	0.2671842	0.2784418
Male	-19.68834	25.03092	-0.790	0.432	-68.74887	29.37218
Comorbidity	-6.66989	22.17813	-0.300	0.764	-50.13895	36.79917
Region 1	Referent Group					
Region 2	-60.91307	46.06072	-1.320	0.186	-151.1919	29.3658
Region 3	-127.6056	48.3572	-2.640	0.008	-222.3855	-32.82562
Region 4	-105.3068	60.53146	-1.740	0.082	-223.9482	13.33473
Region 5	-92.57078	58.42704	-1.580	0.113	-207.0876	21.94603
Region 6	-112.3747	45.06917	-2.490	0.013	-200.7102	-24.03928
Region 7/8	-88.37828	44.61373	-1.980	0.048	-175.8211	-0.9355038
Region 9	-113.4838	52.37079	-2.170	0.030	-216.1304	-10.83725
Region 10	-169.9241	84.30956	-2.020	0.044	-335.1706	-4.677575
Region 11	-233.2797	63.52852	-3.670	< 0.001	-357.7954	-108.764
Non-conus	-1.604393	43.82306	-0.040	0.971	-87.49745	84.28866
Multiple Facilities	206.8548	28.39539	7.280	< 0.001	151.1999	262.5097
Facility Size						
0 to 250	Referent Group					
251 to 500	77.7315	90.98971	0.850	0.393	-100.608	256.071
501 to 1000	78.47808	83.61747	0.940	0.348	-85.4119	242.3681
1001 to 2000	103.8146	74.63487	1.390	0.164	-42.46953	250.0987
2001 to 3000	115.9267	76.05375	1.520	0.127	-33.13843	264.9918
> 3000	262.9103	71.97652	3.650	< 0.001	121.8365	403.984
Dependent of Active Duty	Referent Group					
Retired	165.6446	130.623	1.270	0.205	-90.37619	421.6653
Dependent of Retired	43.16839	33.93307	1.270	0.203	-23.34034	109.6771
Active Duty	-11.87078	38.14051	-0.310	0.756	-86.62607	62.8845
5 to 12 years	Referent Group					
13 to 18 years	-92.01969	33.45923	-2.750	0.006	-157.5997	-26.4397
19 to 40 years	12.84025	30.29124	0.420	0.672	-46.53049	72.21098
Lead Agent	165.3892	34.62345	4.780	< 0.001	97.52738	233.2511
constant	223.9416	82.01254	2.730	0.006	63.19723	384.6859

To test the assumption of equal variance for any fixed combination of covariates in the above least squares regression model, the Cook-Weisberg test for heteroscedasticity was used. Based on the results of this test, the model did not meet the assumption for

homoscedasticity. The results from the Cook-Weisberg test are presented in Table 4.13.

According to Diehr and associates, a potential explanation for not meeting the

homoscedasticity assumption is the presence of multiple outliers in the data.(206)

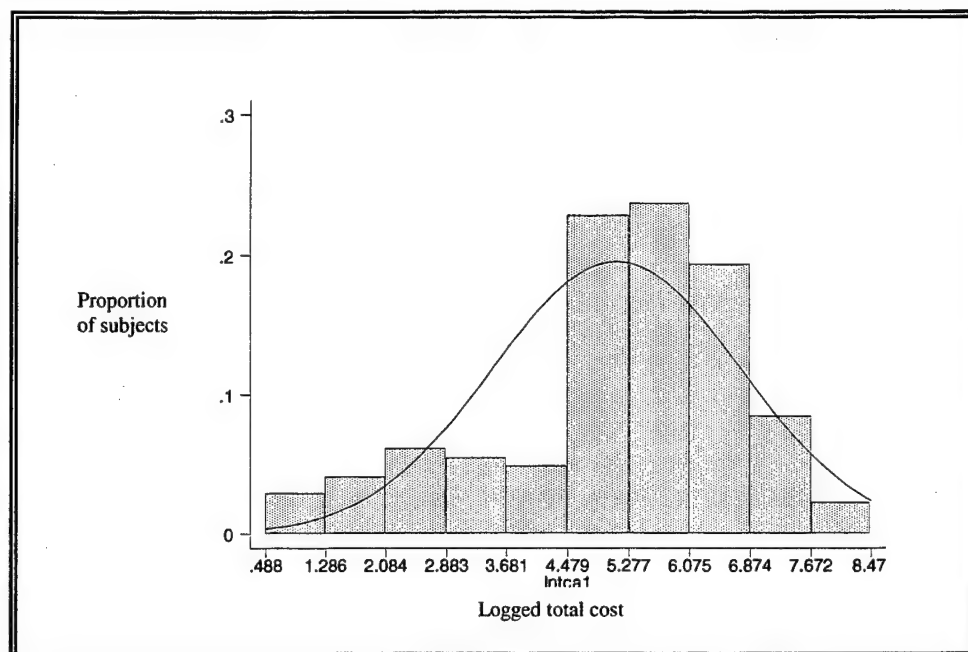
Trimming the cost data at the 99th and 95th percentiles had little effect in reducing the heteroscedasticity of the model. Winsorizing the data so that all data points beyond the 99th and 95th percentile received the 99th and 95th percentile values respectively, also had little effect on the overall homoscedasticity of the model.

To control for the possible effects that the number of prescriptions and visits in the before period might have on the results, the model was run with these covariates added. As with the previous model, the assumption for homoscedasticity was not met ($p < 0.0001$). The model was significant at a level of $p < 0.0001$ with an F -statistic of 340.84. In this model, the use of a formalized CPG use process remained significant ($p < 0.001$) and negative in predicting total asthma costs. The decrease in treatment costs associated with the use of CPGs changed only slightly between the models. With the addition of the covariates for the number of prescriptions and visits in the before period, the beta coefficient for CPG use decreased from \$55.65 to \$54.40. Although there was some variation in coefficient values between the models, there were only two instances in which the significance of a variable was altered. The cost associated with receiving treatment in TRICARE region nine dropped from \$113.48 ($p = 0.030$) to \$91.09 ($p = 0.082$) and in region ten from \$169.92 to \$163.28 ($p = 0.053$), as compared to region one.

The covariate coefficients and p-values for model containing the variables for the number of prescriptions and visits in the before period is presented in Appendix G.

A log transformation of the dependent variable was the next approach used to analyze the effects of CPG on total asthma cost. According to Diehr, transformation of utilization data with a log scale can have several beneficial effects. First, it can shorten the length of the right tail of the distribution, second it can decrease heteroscedasticity, and third it has the potential to decrease the effect of outliers.(206) Before transforming the cost data to a log scale, observations with a cost of zero were modified using a technique suggested by Diehr, in which \$1.00 was added to all total cost observations.(206) This resulted in 97 observations in the after period and 71 observations in the before period being changed from zero to \$1.00. As compared to the untransformed model, the distribution of the dependent variable in this model approaches the shape of a normal distribution as shown in Figure 4.3.

Figure 4.3: Distribution logged total therapy cost after asthma CPG implementation



Independent variables used in the log transformed model were the same as those used in the previous model with the exception the variable for 'total costs before CPG implementation' was log transformed to be consistent with the dependent variable. As with the previous model, the overall log-transformed model was significant with an $F = 114.57$, $p < 0.0001$. The R^2 for this model was considerably lower than the previous model (0.0398) as was the adjusted R^2 (0.0395). The coefficients, p-values, and 95% confidence levels of the independent variables used in the model are presented in Table 4.11.

Table 4.11: OLS regression model predicting log-transformed costs in the after period

Variable	Coefficient	Std Error	t-value	p-value	95% CI	
cpg	-0.06116	0.014017	-4.36	< 0.001	-0.08864	-0.0336926
Total cost before	-0.04877	0.00384	-12.70	< 0.001	-0.0563	-0.0412427
Males	0.045045	0.014569	3.09	< 0.001	0.01649	0.0735997
Comorbidity	0.057099	0.012924	4.42	< 0.001	0.031768	0.0824296
Region 1	Referent category					
Region 2	0.064969	0.026814	2.42	0.015	0.012415	0.1175232
Region 3	-0.14309	0.028146	-5.08	< 0.001	-0.19826	-0.0879256
Region 4	0.006291	0.035233	0.18	0.858	-0.06277	0.0753473
Region 5	-0.00178	0.034006	-0.05	0.958	-0.06843	0.0648687
Region 6	-0.13753	0.026244	-5.24	< 0.001	-0.18897	-0.0860922
Region 7/8	-0.03856	0.025969	-1.48	0.138	-0.08946	0.0123409
Region 9	0.020912	0.030517	0.69	0.493	-0.0389	0.0807251
Region 10	-0.19609	0.049077	-4.00	< 0.001	-0.29228	-0.0999035
Region 11	-0.16708	0.036975	-4.52	< 0.001	-0.23955	-0.0946072
Non-conus	0.002593	0.025506	0.10	0.919	-0.0474	0.0525843
Multiple Facilities	0.697785	0.016693	41.8	< 0.001	0.665068	0.7305022
Facility Size	Referent category					
0 to 250	Referent category					
251 to 500	0.222162	0.052959	4.19	< 0.001	0.118362	0.3259627
501 to 1000	0.324704	0.04867	6.67	< 0.001	0.229312	0.4200961
1001 to 2000	0.385055	0.043442	8.86	< 0.001	0.299909	0.4702011
2001 to 3000	0.510927	0.044269	11.54	< 0.001	0.42416	0.5976948
> 3000	0.660164	0.041908	15.75	< 0.001	0.578025	0.7423025
Dependent of Active Duty	Referent category					
Retired	0.138266	0.076032	1.82	0.069	-0.01076	0.2872876
Dependent of Retired	0.031528	0.019752	1.60	0.11	-0.00719	0.070241
Active Duty	-0.12306	0.022199	-5.54	< 0.001	-0.16657	-0.0795497
5 to 12 years	Referent category					
13 to 18 years	-0.28549	0.019484	-14.65	< 0.001	-0.32368	-0.2473064
19 to 40 years	-0.03839	0.017628	-2.18	0.029	-0.07294	-0.0038338
Lead Agent	0.165988	0.020168	8.23	< 0.001	0.126459	0.2055171
constant	4.751036	0.051611	92.06	< 0.001	4.649879	4.852193

All variables observed as being significant in the initial model remained significant in the log-transformed model. In particular, the formal implementation of the CPG-use process was significant ($p < 0.001$). In addition, the log-transformed model suggested that males

were associated with significantly higher asthma costs than females ($p < 0.001$) and that subject's with comorbid respiratory diseases have higher asthma costs than those without comorbid respiratory diseases ($p < 0.001$). The log-transformed model also suggested significantly lower asthma costs for active duty personnel as compared to dependents of active duty ($p < 0.001$). It is also interesting to note that there was a significant increase in log facilities with greater than 250 observations. In the previous model, facility size was only significantly different between the referent group and facilities with over 3000 observations. Similarly to the previous model, the log-transformed model also suggested significant log-cost differences based upon subject age. Subjects between the age of five and 12 had significantly higher log-costs compared to those older than 18 years of age and those between the ages of 13 to 18. Differences in log-cost based on TRICARE region were similar to the previous model with the exception of region two (mid-atlantic), which was significantly associated with higher log-costs than the referent region (northeast).

As with the initial model, the log-transformed model did not meet the assumption for homoskedasticity as indicated by a χ^2 value of 748.15 ($p < 0.0001$) for the Cook-Weisberg test for heteroscedasticity. Although still significant, the χ^2 value for Cook-Weisberg test for heteroscedasticity improved greatly by removing the independent variables for care received at a lead agent facility and at multiple facilities ($\chi^2 = 186.21, p < 0.0001$), and even further by removing the independent variable indicating a comorbid respiratory condition ($\chi^2 = 116.01, p < 0.001$). Removing additional independent

variables from the model did not improve the results of the Cook-Weisberg test for heteroscedasticity. In both model iterations in which independent variables were removed from the model, the presence of a formal CPG use process remained significant as a predictor of costs associated with providing asthma therapy, however in both instances the model R^2 was lower at 0.0148 and 0.0153 respectively. The coefficients and statistics for the model in which the variables for care at multiple facilities, care at a lead agent facility, and the presence of comorbidities are removed are presented in Table 4.12.

Table 4.12: OLS regression predicting log-transformed costs in the after period with variables for multiple facilities, lead agent, and comorbid respiratory conditions removed

<i>Variable</i>	<i>Coefficient</i>	<i>Std Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Intervals</i>	
cpg	-0.0321459	0.0141358	-2.270	0.023	-0.059852	-0.0044398
Total cost before	-0.0237318	0.0038421	-6.180	< 0.001	-0.0312623	-0.0162012
Males	0.0387191	0.0147522	2.620	0.009	0.0098049	0.0676333
Region 1	Referent Group					
Region 2	0.1206057	0.0270396	4.460	< 0.001	0.0676081	0.1736033
Region 3	-0.1407924	0.0285003	-4.940	< 0.001	-0.1966529	-0.0849318
Region 4	0.0068687	0.0356488	0.190	0.847	-0.0630028	0.0767403
Region 5	-0.0114398	0.0344098	-0.330	0.740	-0.0788829	0.0560033
Region 6	-0.1266576	0.026573	-4.770	< 0.001	-0.1787406	-0.0745746
Region 7/8	-0.0699995	0.0262761	-2.660	0.008	-0.1215005	-0.0184985
Region 9	0.0607223	0.0307851	1.970	0.049	0.0003835	0.121061
Region 10	-0.1512773	0.0487279	-3.100	0.002	-0.2467838	-0.0557708
Region 11	-0.1487878	0.036862	-4.040	< 0.001	-0.2210371	-0.0765385
Non-conus	0.0219406	0.0258107	0.850	0.395	-0.0286483	0.0725295
Facility Size						
0 to 250	Referent Group					
251 to 500	0.2160961	0.0536288	4.030	< 0.001	0.1109839	0.3212084
501 to 1000	0.2797382	0.0492744	5.680	< 0.001	0.1831605	0.3763159
1001 to 2000	0.3185156	0.0439637	7.240	< 0.001	0.2323469	0.4046843
2001 to 3000	0.4349998	0.0447938	9.710	< 0.001	0.3472041	0.5227956
> 3000	0.6118892	0.0421673	14.510	< 0.001	0.5292414	0.694537
Dependent of Active Duty	Referent Group					
Retired	0.0874686	0.0769675	1.140	0.256	-0.0633876	0.2383247
Dependent of Retired	-0.0337428	0.0199006	-1.700	0.090	-0.072748	0.0052623
Active Duty	-0.0686904	0.0224437	-3.060	0.002	-0.11268	-0.0247008
5 to 12 years	Referent Group					
13 to 18 years	-0.3016431	0.0197262	-15.290	< 0.001	-0.3403064	-0.2629798
19 to 40 years	-0.0357636	0.0178509	-2.000	0.045	-0.0707513	-0.0007759
constant	4.792825	0.0522272	91.770	< 0.001	4.69046	4.89519

As noted in Table 4.13, regardless of the type of ordinary least square (OLS) model used, none was found in which the assumption for homoskedasticity was met.

Table 4.13: Cook-Weisberg test for heteroscedasticity using fitted values of total cost after CPG implementation

	<i>Untransformed</i>	<i>Untransformed with utilization variables</i>	<i>Log- transformed</i>	<i>Windsorized at 95%</i>	<i>Windsorized at 99%</i>
χ^2 value	14947840.09	441	748	14396.04	145080.15
p-value	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001

One of the concerns with this data was the presence of extreme outliers and the influence these outliers had on the rest of the data. OLS tends to track and fit outliers, but does so at the expense of the rest of the data. Over the long run this can lead to significant sample-to-sample variation. A robust regression technique developed by Hamilton uses a regression model to calculate case weights based on absolute residuals. The technique then utilizes the new weights to regress the next model to predict new case weights. This process continues until the maximum change in weights drops below tolerance.(208)

This approach, an iteratively reweighted least squares (IRLS) procedure, tends to deal comfortably with outliers unless there is high leverage. Observations with a high degree of leverage are those that not only have unusually high 'x' values, but also have unusually high 'y' values.(209)

Weights for the IRLS approach are derived from one of two weight functions, Huber weights and biweights. Huber weights are used until convergence and then, based on that result, biweights are used until convergence. Both weighting functions are used because Huber weights have problems dealing with severe outliers while biweights sometimes fail

to converge or have multiple solutions. In Huber weighting, cases with small residuals receive weights of one while cases with larger residuals are given gradually smaller weights. In the biweight method, all cases with non-zero residuals receive some downweighting, according to the smoothly decreasing biweight function.(209)

Applying the IRLS technique to the log-transformed cost data provided a model with nearly normally distributed residuals as seen by the histogram in Figure 4.4 and the Q-Q-plot in Figure 4.5. A straight line in the Q-Q plot is representative of data corresponding to a normal distribution. Consistent with the previous OLS models, the findings in this model also suggested that the use of a formal CPG use process was associated with decreased asthma costs.

Figure 4.4: Distribution of total cost residuals in period after CPG implementation using IRLS log-transformed model

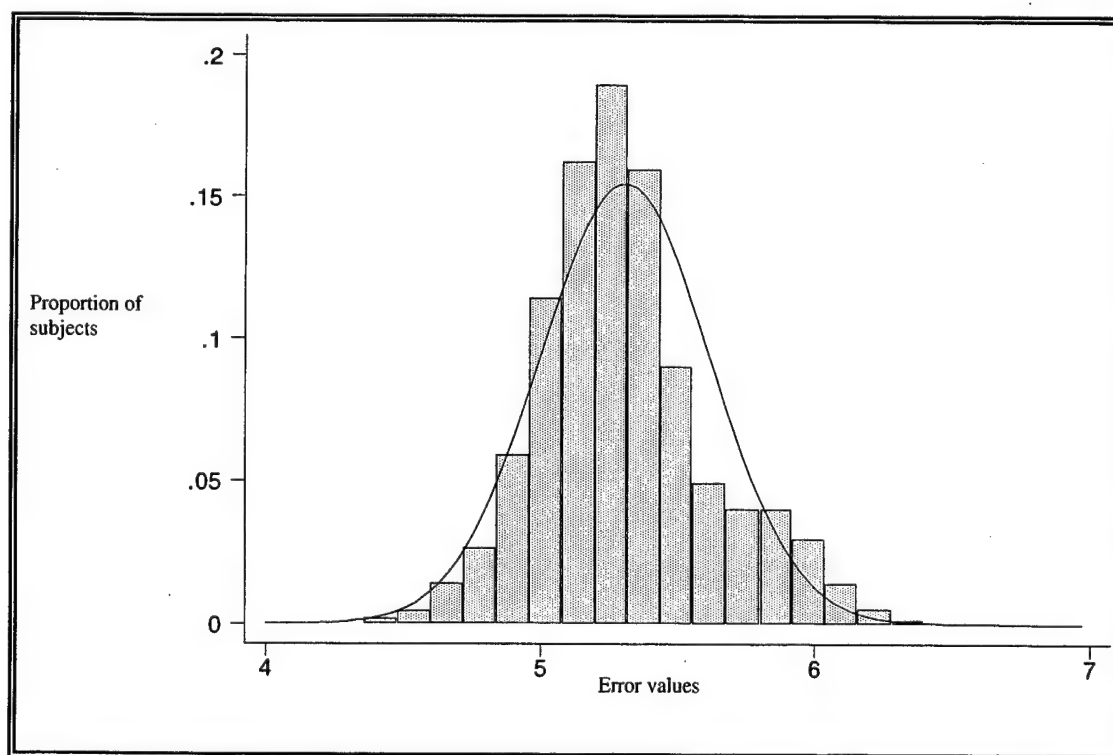
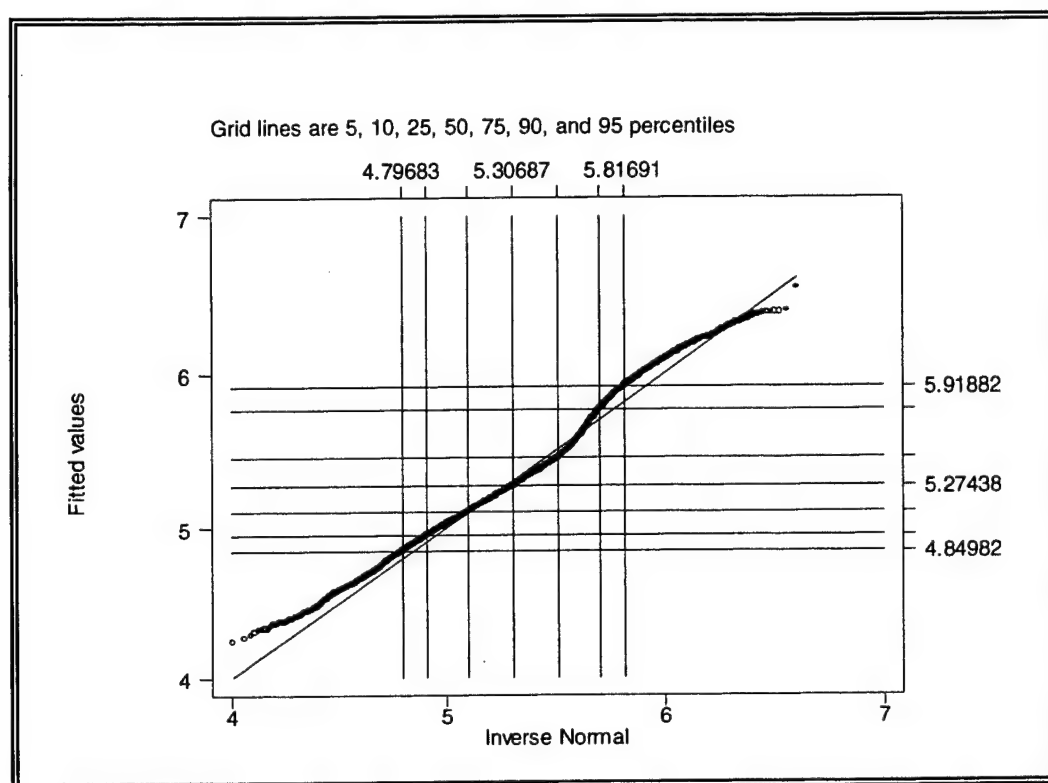


Figure 4.5: Quantile-Quantile (Q-Q) plot for total cost residuals in period after CPG implementation for IRLS log-transformed model



The coefficients and statistics for the independent variables of the IRLS are presented in Table 4.14. As compared with the original log-transformed OLS model, several notable changes occurred in the direction of the coefficients in a number of variables. These variables are indicated with an asterisk (*) next to the variable name. Of the variables in which the coefficients changed directions, none had a significant p-value.

Table 4.14: IRLS regression model predicting log-transformed costs in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% confidence interval</i>	
Cpg	-0.0577583	0.0134826	-4.280	< 0.001	-0.0841841	-0.0313324
Total cost before	-0.0341933	0.0036941	-9.260	< 0.001	-0.0414337	-0.0269529
Males	0.0417973	0.014014	2.980	0.003	0.0143299	0.0692646
Comorbidity*	-0.0044624	0.0124317	-0.360	0.720	-0.0288284	0.0199037
Region 1	Referent Group					
Region 2	0.0650976	0.0257921	2.520	0.012	0.0145451	0.1156501
Region 3	-0.1440022	0.0270738	-5.320	< 0.001	-0.1970667	-0.0909376
Region 4	0.0141284	0.033891	0.420	0.677	-0.0522978	0.0805546
Region 5*	0.0176382	0.0327104	0.540	0.590	-0.046474	0.0817504
Region 6	-0.1401872	0.0252439	-5.550	< 0.001	-0.1896653	-0.0907092
Region 7/8	-0.0376893	0.0249799	-1.510	0.131	-0.0866498	0.0112711
Region 9	0.0096889	0.0293544	0.330	0.741	-0.0478456	0.0672233
Region 10	-0.2194746	0.0472074	-4.650	< 0.001	-0.3120009	-0.1269482
Region 11	-0.1454891	0.035567	-4.090	< 0.001	-0.2152003	-0.075778
Non-conus*	-0.0121271	0.0245342	-0.490	0.621	-0.060214	0.0359598
Multiple Facilities	0.6070042	0.0160567	37.800	< 0.001	0.5755332	0.6384752
Facility Size						
0 to 250	Referent Group					
251 to 500	0.2075449	0.0509421	4.070	< 0.001	0.1076985	0.3073914
501 to 1000	0.343796	0.0468157	7.340	< 0.001	0.2520374	0.4355547
1001 to 2000	0.3816305	0.0417871	9.130	< 0.001	0.2997278	0.4635331
2001 to 3000	0.5094348	0.0425829	11.960	< 0.001	0.4259725	0.5928971
> 3000	0.6429887	0.0403114	15.950	< 0.001	0.5639786	0.7219989
Dependent of Active Duty	Referent Group					
Retired	0.2114062	0.0731354	2.890	0.004	0.0680611	0.3547513
Dependent of Retired	0.0332645	0.0189993	1.750	0.080	-0.003974	0.070503
Active Duty	-0.0621546	0.0213538	-2.910	0.004	-0.1040081	-0.0203012
5 to 12 years	Referent Group					
13 to 18 years	-0.2991853	0.0187417	-15.960	< 0.001	-0.335919	-0.2624516
19 to 40 years	-0.0738804	0.0169568	-4.360	< 0.001	-0.1071156	-0.0406452
Lead Agent	0.1337718	0.0193998	6.900	< 0.001	0.0957482	0.1717954
_con	4.947013	0.0496447	99.650	< 0.001	4.849709	5.044316

Another technique used to analyze the association between asthma CPGs and total costs was a logistic model in which costs in the period after CPG implementation were dichotomized into 'low' and 'high' cost groups. For model balance, total asthma costs

prior to CPG exposure were also added to the model as a dichotomous independent variable. Total costs were considered high if they were greater than \$530 in the period after CPG implementation and greater than \$600 in the period before CPG implementation. This represented the last quartile of cost data for both variables. The 75th percentile was selected as the cut point because of the high degree of right-skewness to the cost data. Other than the cost data, all the other independent variables were the same as those used in the previous OLS models.

This model was consistent with the previous models in regards to the effect of the formal CPG-use process on total costs. Subjects exposed to the CPG-use process were less likely to be in the high-cost treatment group as compared to subjects not treated with the formal CPG-use process (OR = 0.92, CI: 0.88 to 0.95). Factors significantly associated with decreasing asthma costs in this model included the use of a formalized CPG use process, receiving care in TRICARE regions three (Southeast), six (Southwest), ten (Golden Gate), and eleven (Northwest) and being in the 13 to 18 year age category. Factors significantly associated with increased asthma costs included receiving asthma care in multiple facilities or receiving care in a larger facility. These results are consistent with those of the prior analyses and are presented in Table 4.15. No improvement in the goodness-of-fit test was observed when variables for comorbidity, care received at lead agent facilities, and care received at multiple facilities were dropped.

Table 4:15: Logistic regression model dichotomized into 'high' and 'low' cost groups

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% confidence interval</i>	
Cpg	0.9188	0.018	-4.300	<0.001	0.884	0.955
Cost - before	2.4056	0.046	45.910	<0.001	2.317	2.497
Males	1.0284	0.021	1.370	0.172	0.988	1.071
Comorbidity	0.8868	0.016	-6.660	<0.001	0.856	0.919
Region 1	Referent					
Region 2	1.0427	0.039	1.120	0.261	0.969	1.122
Region 3	0.8298	0.034	-4.610	<0.001	0.766	0.898
Region 4	0.9241	0.046	-1.600	0.109	0.839	1.018
Region 5	0.9742	0.046	-0.560	0.577	0.889	1.068
Region 6	0.8681	0.032	-3.830	<0.001	0.808	0.933
Region 7/8	0.9454	0.035	-1.540	0.124	0.880	1.016
Region 9	0.9455	0.041	-1.300	0.193	0.869	1.029
Region 10	0.8138	0.057	-2.960	0.003	0.710	0.933
Region 11	0.8739	0.045	-2.600	0.009	0.790	0.967
Non-conus	1.0655	0.038	1.770	0.077	0.993	1.143
Multiple Facilities	1.7236	0.038	24.970	<0.001	1.651	1.799
0 to 250	Referent					
251 to 500	1.1800	0.099	1.970	0.048	1.001	1.391
501 to 1000	1.3505	0.104	3.910	<0.001	1.162	1.570
1001 to 2000	1.3535	0.094	4.370	<0.001	1.182	1.550
2001 to 3000	1.6709	0.117	7.350	<0.001	1.457	1.916
> 3000	1.9962	0.133	10.360	<0.001	1.752	2.275
Dependent of Active duty	Referent					
Retired	1.2300	0.124	2.060	0.039	1.010	1.498
Dependent of Retired	1.0233	0.029	0.820	0.413	0.968	1.081
Active Duty	0.9756	0.030	-0.790	0.428	0.918	1.037
5 to 12 years	Referent					
13 to 18 years	0.6733	0.019	-13.680	<0.001	0.636	0.713
19 to 40 years	0.9166	0.023	-3.540	<0.001	0.873	0.962
Lead agent	1.2264	0.033	7.620	<0.001	1.164	1.292

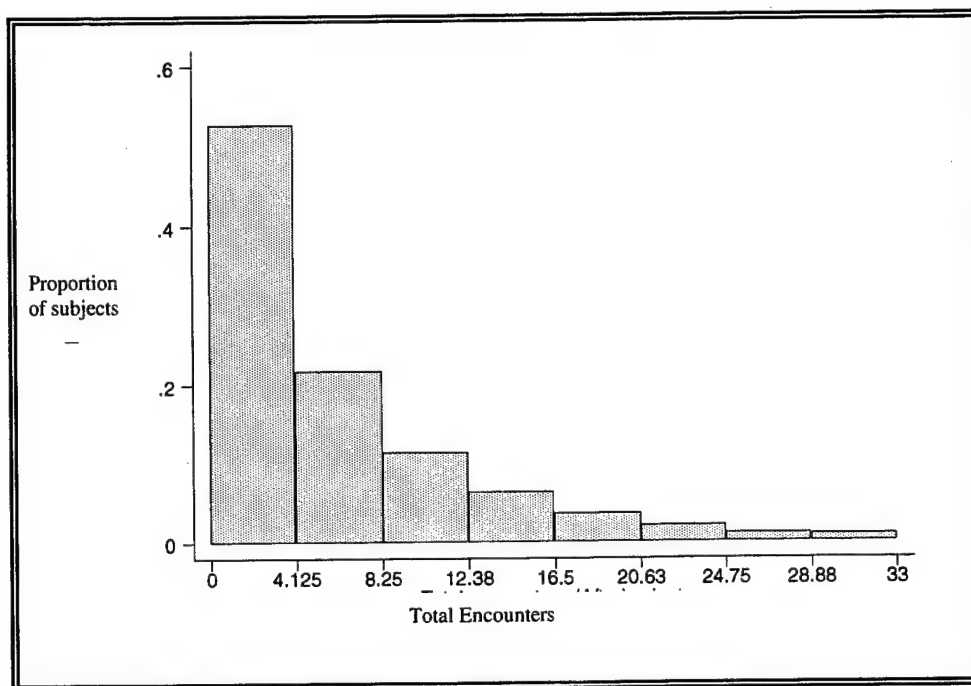
In each OLS iteration of the total cost model, CPG exposure was significantly associated with lower total cost. Although some caution is warranted in interpreting the results of these models due the failure to meet the homoskedasticity assumption, similar results were achieved with the logistic regression model and with the IRLS model in which a normal distribution of the residuals was demonstrated. For these reasons, $H_0:1$ was rejected.

4.4.2 Health care encounters

Ho: 2: There is no difference in the number of asthma related health care encounters experienced by subjects, in the periods before and after exposure to the CPG-use process.

The distribution health care encounters for asthma subjects, similarly to that of the cost data, was skewed heavily to the right as noted in Figure 4.6.

Figure 4.6: OLS untransformed model: Distribution of total health care encounters



The mean number of encounters per subject was 6.60 ± 6.96 with a minimum of one and a maximum of 80. The median number of encounters was four. Because of similar appearance between the distributions of the cost and encounter data, the same approach used to analyze the cost data was used for this analysis.

The overall untransformed model was significant ($p < 0.0001$) with an F statistic of 1088. The R^2 was nearly 29 percent, suggesting this model did a reasonably good job of explaining the factors responsible for asthma related health care encounters.

The use of a formal CPG use process was not significantly related to the total number of health care encounters ($p = 0.143$). Five factors in the model were associated with a

significant increase in health care encounters. They were: 1) the male gender ($p < 0.0001$); 2) subjects receiving care in the Mid-Atlantic or non-continental TRICARE regions as compared to the Northeast region ($p < 0.0001$); 3) subjects receiving care in multiple facilities ($p < 0.001$); 4) subjects receiving care in any facilities with more than 250 observations ($p < 0.011$ to $p < 0.0001$); and 5) dependents of military retirees as compared to dependents of active duty personnel.

Four factors in the model were significantly associated with fewer health care encounters per subject. These included: 1) the presence of a comorbid respiratory condition; 2) care received in the Northwest, as compared to the Northeast TRICARE region; 3) an active duty beneficiary status as compared to a status of dependent of active duty; and 4) being in the 13 to 18 year age category as compared to the 12 and under age group. Although it appears counter-intuitive that those with a comorbid respiratory condition would have fewer health care encounters than those diagnosed only with asthma, one possible explanation for this might be that for those with multiple diagnoses, asthma related encounters are sometimes mistakenly miscoded with an alternative diagnosis.

The variable coefficients and statistics for total health encounters (untransformed) are presented in Table 4.16. The assumption of homoskedasticity for this model was not met, as the Cook-Weisberg test for heteroscedasticity was significant ($p < 0.0001$).

Trimming and windsorizing the most extreme observations at the 99th and 95th percentiles had little effect on the homoskedasticity.

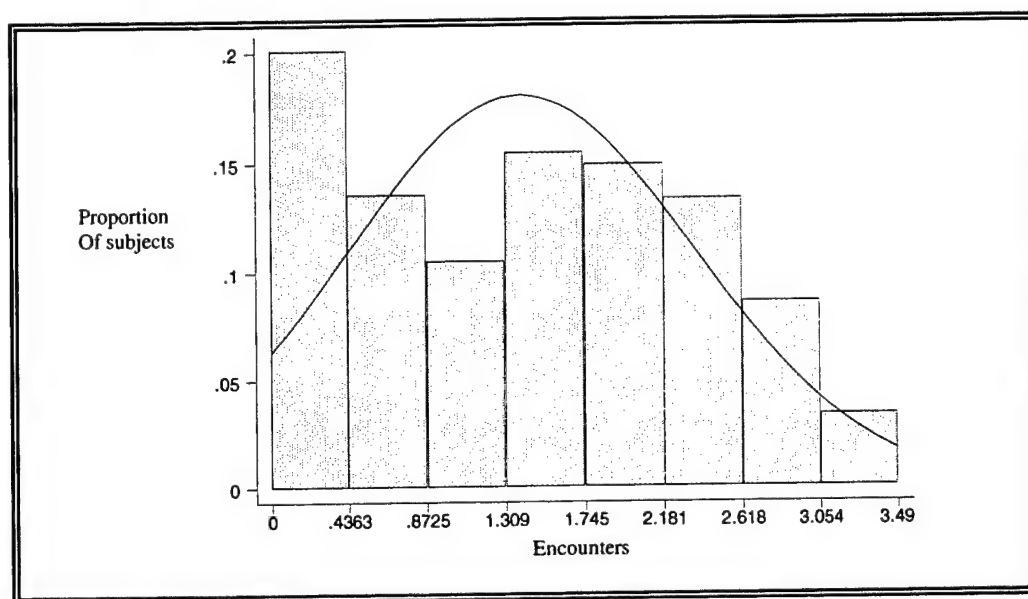
Table 4.16: OLS regression model predicting encounters in the after period

Variable	Coefficient	Std Error	t-value	p-value	95% Confidence Interval	
cpg	0.0714	0.048697	1.470	0.143	-0.0240458	0.1668452
Total encounters before	0.481696	0.002997	160.730	< 0.001	0.475822	0.48757
Males	0.208744	0.050649	4.120	< 0.001	0.1094732	0.3080149
Comorbidity	-0.48898	0.045109	-10.840	< 0.001	-0.577389	-0.4005624
Region 1	Referent Category					
Region 2	0.335892	0.093165	3.610	< 0.001	0.1532882	0.5184959
Region 3	-0.18501	0.097808	-1.890	0.059	-0.3767138	0.0066924
Region 4	-0.07766	0.12243	-0.630	0.526	-0.3176204	0.1623031
Region 5	-0.01549	0.118188	-0.130	0.896	-0.2471385	0.2161577
Region 6	-0.12745	0.091176	-1.400	0.162	-0.3061568	0.0512536
Region 7/8	0.068801	0.090239	0.760	0.446	-0.1080666	0.2456682
Region 9	-0.03081	0.106012	-0.290	0.771	-0.2385888	0.1769761
Region 10	0.016334	0.170528	0.100	0.924	-0.3178999	0.3505684
Region 11	-0.39834	0.128543	-3.100	0.002	-0.6502801	-0.1463931
Non-conus	0.232976	0.08864	2.630	0.009	0.0592416	0.4067101
Multiple Facilities	0.546453	0.057639	9.480	< 0.001	0.4334808	0.6594255
Facility Size						
0 to 250	Referent Category					
251 to 500	0.283646	0.184034	1.540	0.123	-0.0770606	0.644352
501 to 1000	0.427506	0.169123	2.530	0.011	0.0960251	0.7589874
1001 to 2000	0.552573	0.15096	3.660	< 0.001	0.2566926	0.8484531
2001 to 3000	0.587603	0.153831	3.820	< 0.001	0.2860957	0.8891103
> 3000	0.657393	0.145604	4.510	< 0.001	0.3720087	0.9427764
Dependent of Active Duty	Referent Category					
Retired	0.3304	0.264269	1.250	0.211	-0.1875665	0.8483667
Dependent of Retired	0.149551	0.068649	2.180	0.029	0.0149981	0.2841029
Active Duty	-0.48398	0.077157	-6.270	< 0.001	-0.6352039	-0.3327479
5 to 12 years	Referent Category					
13 to 18 years	-0.74248	0.067694	-10.970	< 0.001	-0.8751558	-0.6097946
19 to 40 years	0.117633	0.06126	1.920	0.055	-0.0024353	0.2377018
Lead Agent	0.023995	0.070103	0.340	0.732	-0.1134076	0.1613975
constant	2.703595	0.16705	16.180	< 0.001	2.376178	3.031012

The log-transformation of the encounter variable resulted in a somewhat more normal distribution (Figure 4.7) than the non-transformed model. The overall model was

significant with an F -statistic of 777.08 ($p < 0.0001$). Both the R^2 and adjusted R^2 were somewhat lower than the corresponding values in the non-transformed model.

Figure 4.7 OLS log-transformed model: Distribution of encounters after CPG implementation.



In the log-transformed model, as with the previous model, a formal CPG use process had no significant effect on the total number of health care encounters experienced by subjects with asthma. Consistent with the previous model, factors associated with a significant increase in the number of health care encounters included being of male gender, receiving care in the mid-atlantic region, receiving care in multiple facilities, receiving care in larger MTFs, and being the dependent of a retiree. Variables consistent with the previous model for significantly decreasing health care encounters included the presence of a comorbid respiratory condition, having received care in the northwest region, or being on active duty status. Other variables significant for lowering health care

encounters in this model that were not significant in the previous model included care received in either the Southeast or Southwest regions. Model coefficients and statistics are presented in Table 4.17.

Table 4.17: OLS regression model predicting log-transformed encounters in the after period

<i>Variables</i>	<i>Coefficient</i>	<i>Std Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
cpg	0.0034304	0.0055911	0.610	0.540	-0.0075281	0.0143889
Total encounters before	0.4612895	0.0033092	139.400	< 0.001	0.4548036	0.4677754
Males	0.0367125	0.0058151	6.310	< 0.001	0.0253148	0.0481101
Comorbidity	-0.0822012	0.0052093	-15.780	< 0.001	-0.0924113	-0.0719911
Region 1	Referent Group					
Region 2	0.0404137	0.0106952	3.780	< 0.001	0.0194512	0.0613761
Region 3	-0.0326502	0.0112284	-2.910	0.004	-0.0546579	-0.0106425
Region 4	-0.0172061	0.0140554	-1.220	0.221	-0.0447546	0.0103424
Region 5	-0.0216013	0.0135678	-1.590	0.111	-0.0481942	0.0049916
Region 6	-0.0344022	0.0104675	-3.290	< 0.001	-0.0549186	-0.0138859
Region 7/8	-0.0033543	0.0103599	-0.320	0.746	-0.0236595	0.016951
Region 9	0.0006594	0.0121722	0.050	0.957	-0.023198	0.0245167
Region 10	-0.0007164	0.0195762	-0.040	0.971	-0.0390858	0.0376529
Region 11	-0.0588385	0.0147555	-3.990	< 0.001	-0.0877593	-0.0299178
Non-conus	0.0186613	0.0101758	1.830	0.067	-0.0012832	0.0386057
Multiple Facilities	0.0746748	0.0066222	11.280	< 0.001	0.0616954	0.0876542
Facility Size						
0 to 250	Referent Group					
251 to 500	0.0329949	0.0211276	1.560	0.118	-0.0084152	0.0744049
501 to 1000	0.045092	0.019416	2.320	0.020	0.0070368	0.0831472
1001 to 2000	0.0665261	0.0173308	3.840	< 0.001	0.0325578	0.1004944
2001 to 3000	0.0702071	0.0176604	3.980	< 0.001	0.0355927	0.1048214
> 3000	0.0910402	0.0167152	5.450	< 0.001	0.0582784	0.123802
Dependent of Active Duty	Referent Group					
Retired	0.0511034	0.0303366	1.680	0.092	-0.0083562	0.110563
Dependent of Retired	0.023089	0.0078822	2.930	0.003	0.0076398	0.0385381
Active Duty	-0.0752679	0.0088589	-8.500	< 0.001	-0.0926313	-0.0579045
5 to 12 years	Referent Group					
13 to 18 years	-0.0969839	0.0077725	-12.480	< 0.001	-0.112218	-0.0817499
19 to 40 years	0.005584	0.0070327	0.790	0.427	-0.0082	0.019368
Lead Agent	-0.0024876	0.0080442	-0.310	0.757	-0.0182542	0.013279
constant	0.8528587	0.0199454	42.760	< 0.001	0.8137657	0.8919517

The IRLS regression technique was also used to analyze the encounter data using the log-transformed data. The coefficients and model statistic are presented in Table 4.18 below:

Table 4.18: IRLS regression model predicting log-transformed encounters in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Intervals</i>	
cpg	0.0030081	0.0058316	0.520	0.606	-0.0084217	0.0144379
Total encounters before	0.4929568	0.0034515	142.820	< 0.001	0.4861919	0.4997217
Males	0.0405912	0.0060652	6.690	< 0.001	0.0287034	0.052479
Comorbidity	-0.0901748	0.0054333	-16.600	< 0.001	-0.1008241	-0.0795256
Region 1	Referent group					
Region 2	0.0361572	0.0111552	3.240	< 0.001	0.0142932	0.0580213
Region 3	-0.0390025	0.0117114	-3.330	< 0.001	-0.0619567	-0.0160482
Region 4	-0.0196657	0.0146599	-1.340	0.180	-0.048399	0.0090677
Region 5	-0.0267732	0.0141514	-1.890	0.059	-0.0545099	0.0009635
Region 6	-0.0432763	0.0109178	-3.960	< 0.001	-0.0646751	-0.0218775
Region 7/8	-0.0099739	0.0108054	-0.920	0.356	-0.0311526	0.0112047
Region 9	0.0067042	0.0126957	0.530	0.597	-0.0181793	0.0315876
Region 10	-0.0028583	0.0204182	-0.140	0.889	-0.0428779	0.0371613
Region 11	-0.0539793	0.0153902	-3.510	< 0.001	-0.084144	-0.0238147
Non-conus	0.0098641	0.0106134	0.930	0.353	-0.0109382	0.0306663
Multiple Facilities	0.0790579	0.006907	11.450	< 0.001	0.0655203	0.0925956
Facility Size						
0 to 250	Referent group					
251 to 500	0.0265402	0.0220363	1.200	0.228	-0.0166509	0.0697314
501 to 1000	0.0380536	0.020251	1.880	0.060	-0.0016384	0.0777456
1001 to 2000	0.0626662	0.0180762	3.470	< 0.001	0.027237	0.0980955
2001 to 3000	0.0629322	0.01842	3.420	< 0.001	0.0268291	0.0990353
> 3000	0.0859029	0.0174341	4.930	< 0.001	0.0517321	0.1200738
Dependent of Active Duty	Referent group					
Retired	0.0557378	0.0316414	1.760	0.078	-0.0062792	0.1177547
Dependent of Retired	0.0248844	0.0082213	3.030	0.002	0.0087707	0.040998
Active Duty	-0.0886451	0.0092399	-9.590	< 0.001	-0.1067553	-0.0705349
5 to 12 years	Referent group					
13 to 18 years	-0.0954107	0.0081068	-11.770	< 0.001	-0.1113	-0.0795215
19 to 40 years	0.0061196	0.0073351	0.830	0.404	-0.0082572	0.0204965
Lead Agent	-0.0078787	0.0083902	-0.940	0.348	-0.0243234	0.008566
constant	0.7967188	0.0208033	38.300	< 0.001	0.7559444	0.8374932

As with the OLS models, the formal CPG use process in the IRLS model was not significant for predicting the number of health care encounters. In this model, factors associated with a significant increase in the number of health care encounters included being of male gender, receiving care in TRICARE region two (compared to TRICARE region one), receiving care in multiple facilities, receiving care in larger MTFs, and being the dependent of a retiree (compared to a dependent of active duty). Factors significantly associated with a decrease in health care encounters included the presence of a comorbid respiratory condition, receipt of care in regions three, six, or eleven, being on active duty status, and being between 13 to 18 years of age.

As noted by the histogram in Figure 4.8, the residuals of the log-transformed model do not appear to be normally distributed, as there are more values than expected clustered towards the left side of the distribution. The clustering of values toward the left of the distribution is further illustrated in Figure 4.9 by the divergence of lines in the Q-Q plot. One possible explanation for the failure of the IRLS technique in this model would be the existence of multiple outliers with high leverage.

Figure 4.8: Encounter residuals in the period after CPG implementation from the IRLS log-transformed model.

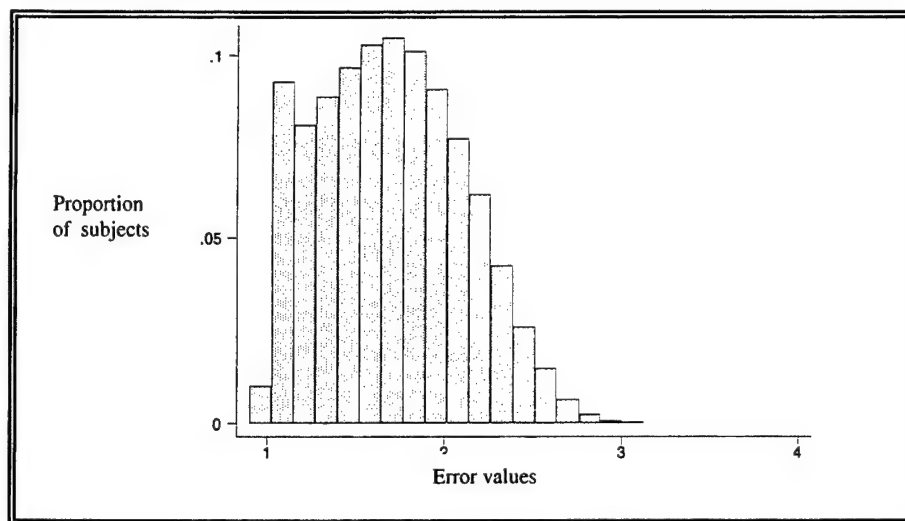
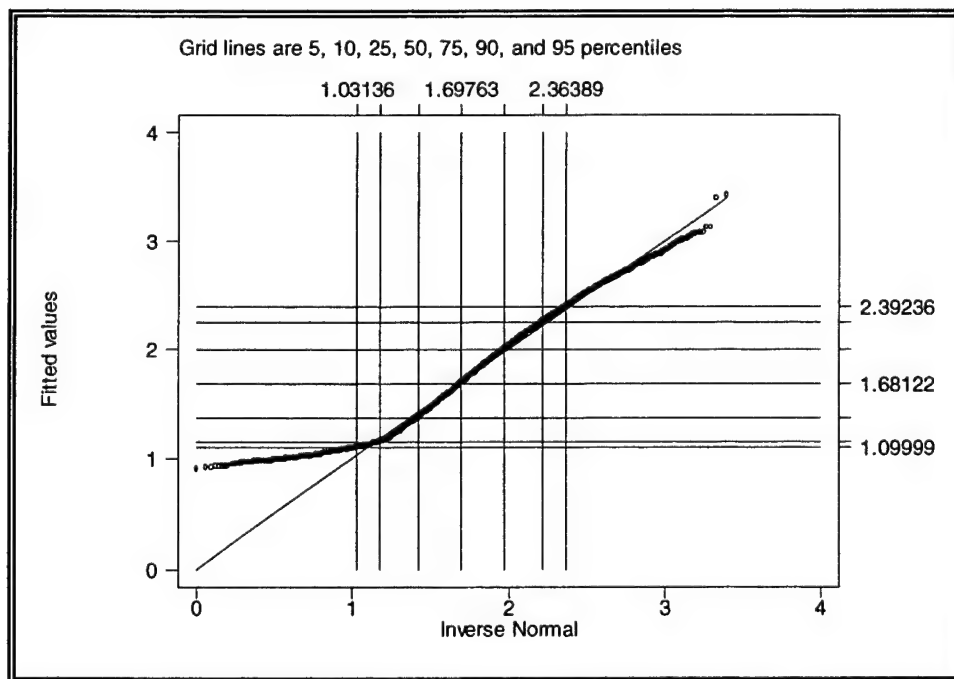


Figure 4.9: Quantile-Quantile (Q-Q) plot for residuals in period after CPG exposure for the IRLS log-transformed model



To further analyze the association between a formal CPG use process in the treatment of asthma and the number of health care encounters, a logistic model was used. The dependent variable was dichotomized such that more than nine encounters in the period after CPG implementation, and more than ten encounters in the group before CPG implementation (75th percentile for both periods), placed the subject in the 'high-encounter' group. The observed association between CPG use and the number of health care encounters remained non-significant. The odds ratio was 0.98 with a p-value of 0.542. Consistent with the findings of the OLS models, the presence of a comorbid respiratory condition was significantly associated with decreased encounters as was being in the 13 to 18 age category and being on active duty status. Receiving care in the southeast, southern California, or northwest TRICARE regions was also associated with significantly fewer health care encounters than the northeast region. Receiving asthma care in the mid-atlantic region was associated with significantly higher number of health care encounters than the reference region (northeast). Other factors in this model that were associated with an increased number of health care encounters was a beneficiary status other than active duty, and a male gender type. Odds ratios and statistics are presented in Table 4.19. The overall model was significant ($p < 0.0001$), however the goodness-of-fit test indicated a poor fit of the data to the model ($p < 0.0001$).

Table 4.19: Logistic regression model for high and low encounter groups.

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.9876433	0.0201486	-0.610	0.542	0.9489318	1.027934
Encounters – High	5.867556	0.1126041	92.200	< 0.001	5.650955	6.092459
Males	1.1295	0.0241105	5.700	< 0.001	1.083219	1.177758
Comorbidity	0.7713315	0.0143943	-13.910	< 0.001	0.7436289	0.8000661
Region 1	Referent Group					
Region 2	1.117045	0.0430649	2.870	0.004	1.035749	1.204721
Region 3	0.917037	0.037968	-2.090	0.036	0.8455603	0.9945557
Region 4	0.9260349	0.0479204	-1.480	0.138	0.8367185	1.024885
Region 5	0.9349673	0.0467251	-1.350	0.178	0.8477301	1.031182
Region 6	0.9624502	0.0366087	-1.010	0.314	0.8933078	1.036944
Region 7/8	1.026786	0.038719	0.700	0.483	0.9536342	1.105548
Region 9	0.8760496	0.0399722	-2.900	0.004	0.8011065	0.9580036
Region 10	0.8887676	0.0642187	-1.630	0.103	0.7714076	1.023983
Region 11	0.7988603	0.044627	-4.020	0.000	0.7160113	0.8912957
Non-conus	1.03677	0.0384449	0.970	0.330	0.9640924	1.114926
Multiple Facilities	1.307439	0.0303531	11.550	< 0.001	1.249281	1.368305
Facility Size						
0 to 250	Referent Group					
251 to 500	1.020094	0.0814582	0.250	0.803	0.8723058	1.192921
501 to 1000	1.033386	0.0759718	0.450	0.655	0.8947141	1.19355
1001 to 2000	1.076027	0.0704668	1.120	0.263	0.9464111	1.223395
2001 to 3000	1.122434	0.0747243	1.730	0.083	0.9851292	1.278875
> 3000	1.169738	0.0738678	2.480	0.013	1.033561	1.323857
Dependent of Active Duty	Referent Group					
Retired	1.268979	0.129572	2.330	0.020	1.03882	1.55013
Dependent of Retired	1.056825	0.0303389	1.930	0.054	0.999004	1.117993
Active Duty	0.8045069	0.0262687	-6.660	< 0.001	0.754634	0.8576758
5 to 12 years	Referent Group					
13 to 18 years	0.7418476	0.0217939	-10.160	< 0.001	0.7003389	0.7858165
19 to 40 years	1.034084	0.0264895	1.310	0.191	0.9834478	1.087328
Lead Agent	1.055305	0.0304024	1.870	0.062	0.9973684	1.116607

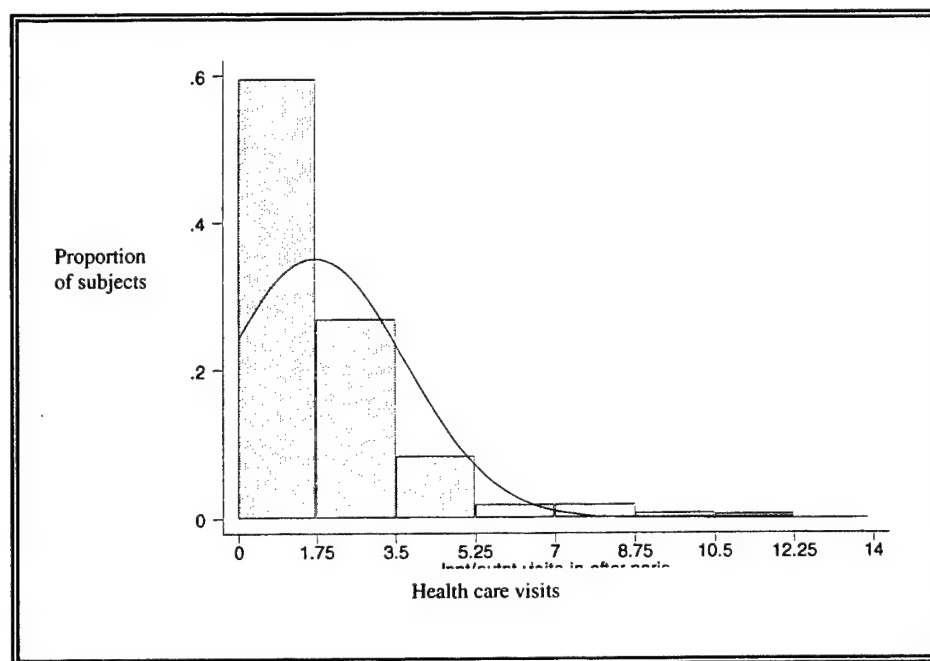
The analyses performed to determine the association between the formal CPG use process and the number of asthma related health care encounters a subject experienced suggested no significant relationship. This result was consistent among all the models used to test the association. For this reason, $H_0: 2$ was not rejected.

4.4.3 Health care visits

Ho: 3: There is no difference, before and after CPG exposure, in the number of asthma related health care visits for subjects with a diagnosis of asthma.

For the purposes of this research, the variable 'visits' was defined as all inpatient and outpatient encounters, excluding prescriptions dispensed. The mean number of total visits was 4.30 ± 4.90 for the total period, 1.90 ± 2.44 for the period before CPG implementation, and 2.39 ± 2.16 for the period after CPG implementation. The range of visits was 1 to 171 for the entire study period, 0 to 129 for the period prior to CPG implementation, and 0 to 63 for the period after CPG implementation. The distribution for visits in the period after CPG exposure is illustrated in Figure 4.10 (truncated at the 99th percentile for display purposes).

Figure 4.10: Distribution of health care visits after CPG implementation



As would be expected, and similar to the cost and encounter data, the majority of subjects experienced a low number (between zero and two) of asthma associated health care visits. This resulted again, in a distribution that was highly skewed to the right. Statistical techniques similar to those used for the cost and encounter variables were used for this analysis.

When prescriptions were excluded, and only inpatient and outpatient visits were considered, the use of a formal CPG use process was associated with a small but significant increase of 0.122 health care visits per subject ($p < 0.001$). Other factors associated with a significant increase in health care visits, when prescriptions were not considered, included the presence of a respiratory comorbidity, receiving care in TRICARE

regions two, nine, or 12, receiving care in multiple facilities, and receiving care in a larger MTF. Factors significantly associated with fewer health care visits included receiving care in TRICARE regions three, seven, and eleven, or being in one of the two older age categories. The overall model was significant with a F -statistic of 256.08 and a p -value less than 0.0001. Consistent with other models using utilization data, the R^2 and adjusted R^2 for this model were quite low at 0.0848 and 0.0845 respectively.(206) The assumption for homoscedasticity, as tested by the Cook-Weisberg test for heteroscedasticity was not met ($p < 0.0001$). As with the cost and encounter variables, trimming the top one and five percent of observations to reduce the effect of outliers, did not change the results of the test. The results of this model are presented in Table 4.20.

Table 4.20: OLS regression model predicting health care visits in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.1222197	0.0234806	5.210	< 0.001	0.0761978	0.1682415
Visits - before	0.2261022	0.0033599	67.290	< 0.001	0.2195168	0.2326876
Males	-0.0513027	0.0244111	-2.100	0.036	-0.0991484	-0.0034571
Comorbidity	0.3991978	0.0216577	18.430	< 0.001	0.3567487	0.4416468
Region 1	Referent Group					
Region 2	0.2191133	0.0449184	4.880	< 0.001	0.1310733	0.3071533
Region 3	-0.2109672	0.0471578	-4.470	< 0.001	-0.3033962	-0.1185381
Region 4	0.1103576	0.0590416	1.870	0.062	-0.0053638	0.226079
Region 5	0.0431732	0.0569855	0.760	0.449	-0.0685183	0.1548646
Region 6	-0.0787842	0.0439688	-1.790	0.073	-0.1649628	0.0073944
Region 7/8	-0.1067121	0.0435118	-2.450	0.014	-0.191995	-0.0214291
Region 9	0.226082	0.051089	4.430	< 0.001	0.1259477	0.3262162
Region 10	0.0603436	0.0822159	0.730	0.463	-0.1007994	0.2214865
Region 11	-0.2295049	0.061967	-3.700	< 0.001	-0.35096	-0.1080499
Non-conus	0.2454387	0.0427388	5.740	< 0.001	0.1616707	0.3292066
Multiple Facilities	0.4940777	0.0278258	17.760	< 0.001	0.4395392	0.5486162
Facility Size						
0 to 250	Referent Group					
251 to 500	0.1570913	0.0887336	1.770	0.077	-0.0168262	0.3310089
501 to 1000	0.292513	0.0815458	3.590	< 0.001	0.1326835	0.4523424
1001 to 2000	0.3726743	0.0727896	5.120	< 0.001	0.2300069	0.5153418
2001 to 3000	0.526898	0.0741736	7.100	< 0.001	0.381518	0.672278
> 3000	0.6955897	0.0702265	9.900	< 0.001	0.557946	0.8332335
Dependent of Active Duty	Referent Group					
Retired	-0.1751742	0.1273912	-1.380	0.169	-0.4248606	0.0745122
Dependent of Retired	-0.005477	0.0330917	-0.170	0.869	-0.0703366	0.0593826
Active Duty	0.0407182	0.0371992	1.090	0.274	-0.032192	0.1136285
5 to 12 years	Referent Group					
13 to 18 years	-0.3589916	0.0326439	-11.000	< 0.001	-0.4229737	-0.2950096
19 to 40 years	-0.1807697	0.0295383	-6.120	< 0.001	-0.2386646	-0.1228748
Lead Agent	-0.0091093	0.0337605	-0.270	0.787	-0.0752797	0.0570612
constant	0.5448532	0.0801233	6.800	< 0.001	0.3878118	0.7018947

Very little difference in the overall results of the model were noted when the dependent variable (visits after CPG implementation) and the corresponding independent variable for visits before CPG implementation, were log transformed. The association between

total visits and CPG use was almost identical between the two permeations of the model. The only notable difference between the model variables was with TRICARE region two. In the log-transformed permeation of the model, region two (mid-atlantic) was no longer significantly associated with increased asthma visits. The R^2 and adjusted R^2 dropped slightly in the log-transformed model to 0.0517 and 0.0513 respectively. The overall log-transformed model was significant with an F -statistic of 150.57 ($p < 0.0001$). The assumption for homoscedasticity, as tested by the Cook-Weisberg test for heteroscedasticity was not met ($p < 0.0001$). The coefficients and model statistics are presented in Table 4.21.

Table 4.21: OLS regression model predicting log-transformed visits in the after period

<i>Variable</i>	<i>Coefficient.</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0203914	0.0054152	3.770	< 0.001	0.0097775	0.0310052
Visits - before	-0.034489	0.0037773	-9.130	< 0.001	-0.0418924	-0.0270856
Males	-0.0138413	0.0056306	-2.460	0.014	-0.0248772	-0.0028053
Comorbidity	0.1471967	0.0049922	29.490	< 0.001	0.1374121	0.1569814
Region 1	Referent group					
Region 2	0.0137475	0.0103612	1.330	0.185	-0.0065604	0.0340554
Region 3	-0.0690407	0.010877	-6.350	< 0.001	-0.0903596	-0.0477218
Region 4	0.0198082	0.0136171	1.450	0.146	-0.0068813	0.0464977
Region 5	-0.0010769	0.0131415	-0.080	0.935	-0.0268342	0.0246805
Region 6	-0.0558113	0.0101465	-5.500	< 0.001	-0.0756983	-0.0359243
Region 7/8	-0.028553	0.0100371	-2.840	0.004	-0.0482256	-0.0088803
Region 9	0.0619292	0.0117861	5.250	< 0.001	0.0388286	0.0850298
Region 10	-0.0032183	0.018963	-0.170	0.865	-0.0403856	0.0339491
Region 11	-0.0551715	0.0142899	-3.860	< 0.001	-0.0831795	-0.0271634
Non-conus	0.0502978	0.0098577	5.100	< 0.001	0.0309767	0.0696189
Multiple Facilities	0.2647965	0.0064637	40.970	< 0.001	0.2521276	0.2774654
Facility Size						
0 to 250	Referent group					
251 to 500	0.0500738	0.0204662	2.450	0.014	0.0099601	0.0901876
501 to 1000	0.1086777	0.0188084	5.780	< 0.001	0.0718133	0.1455422
1001 to 2000	0.1438363	0.0167888	8.570	< 0.001	0.1109303	0.1767423
2001 to 3000	0.1717161	0.0171075	10.040	< 0.001	0.1381854	0.2052468
> 3000	0.2433358	0.0161951	15.030	< 0.001	0.2115935	0.2750782
Dependent of Active Duty	Referent group					
Retired	-0.083462	0.0293811	-2.840	0.005	-0.1410489	-0.025875
Dependent of Retired	-0.0121562	0.0076325	-1.590	0.111	-0.0271159	0.0028035
Active Duty	-0.0086126	0.0085787	-1.000	0.315	-0.0254268	0.0082017
5 to 12 years	Referent group					
13 to 18 years	-0.1285112	.0075315	17.060	< 0.001	-0.143273	-0.1137494
19 to 40 years	-0.0877982	.0068146	12.880	< 0.001	-0.1011548	-0.0744417
Lead Agent	-0.0246151	0.0077859	-3.160	0.002	-0.0398754	-0.0093548
constant	0.5729488	0.0186985	30.640	< 0.001	0.5362997	0.6095978

A logistic model also was used to analyze the association between CPG use and the number of health care visits experienced by subjects due to asthma. Visits in the after period were dichotomized at the 75th percentile such that anyone with two or more visits

was considered to be in the high-visit group and those with less than two visits in the low-visit group. Similarly, the cut point for the before period was at the 75th percentile, which in this case was three visits. Consistent with the OLS models, there was a small but significant increase in the risk of experiencing a higher number of asthma related health care visits upon exposure to the CPG use process (OR = 1.05; 95% CI: 1.01 to 1.08). Factors significantly associated with a higher number of health care visits included having a respiratory comorbidity (OR = 1.43; 95% CI: 1.39 to 1.48), receiving asthma therapy at more than one treatment facility (OR = 1.86; 95% CI: 1.79 to 1.93), receiving care in facilities with more than 500 observations (for range of odds ratios see Table 4.22), and receiving care in region nine (OR = 1.16; 95% CI: 1.08 to 1.25) or outside of the continental U.S. (OR = 1.08; 95% CI: 1.02 to 1.15). Factors associated with fewer asthma related visits included: receiving care at a lead agent facility (OR = 0.92; 95% CI: 0.87 to 0.96), age between 19 to 40 years (OR = 0.76; 95% CI: 0.73 to 0.80), age between 13 to 18 (OR = 0.69; 95% CI: 0.66 to 0.72); a retired beneficiary status (OR = 0.79; 95% CI: 0.60 to 0.96), care received in TRICARE region eleven (OR = 0.89; 95% CI: 0.82 to 0.97), care received in TRICARE regions seven and eight (OR = 0.90; 95% CI: 0.85 to 0.96); care received in TRICARE region six (OR = 0.82; 95% CI: 0.77 to 0.87), and care received in TRICARE region three (OR = 0.82; 95% CI: 0.76 to 0.87). The results for the model are presented in Table 4.22. The goodness-of-fit test ($p = 0.0006$) for this model suggested a poor fit between the data and model.

Table 4.22: Logistic regression for high and low health care visits

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	1.046505	0.0178988	2.660	0.008	1.012005	1.082181
Visits - before	1.259151	0.0210183	13.800	< 0.001	1.218623	1.301028
Males	0.9667567	0.0171947	-1.900	0.057	0.9336364	1.001052
Comorbidity	1.434744	0.0227622	22.750	< 0.001	1.390818	1.480058
Region 1	Referent Category					
Region 2	0.9608489	0.031373	-1.220	0.221	0.9012851	1.024349
Region 3	0.8160421	0.0282286	-5.880	< 0.001	0.7625489	0.8732879
Region 4	0.9820684	0.0421145	-0.420	0.673	0.9028993	1.068179
Region 5	0.9515922	0.0393116	-1.200	0.230	0.8775797	1.031847
Region 6	0.8171005	0.0262239	-6.290	< 0.001	0.7672857	0.8701493
Region 7/8	0.9074153	0.0287351	-3.070	0.002	0.8528077	0.9655196
Region 9	1.162487	0.0429753	4.070	< 0.001	1.081237	1.249844
Region 10	0.9676612	0.0581825	-0.550	0.585	0.8600885	1.088688
Region 11	0.8922109	0.0403403	-2.520	0.012	0.8165474	0.9748857
Non-conus	1.085205	0.0336779	2.630	0.008	1.021165	1.153261
Multiple Facilities	1.857479	0.0371851	30.930	< 0.001	1.786009	1.931809
Facility Size						
0 to 250	Referent Category					
251 to 500	1.138903	0.0769159	1.930	0.054	0.9977022	1.300088
501 to 1000	1.372798	0.0847668	5.130	< 0.001	1.216318	1.54941
1001 to 2000	1.423672	0.0790952	6.360	< 0.001	1.276791	1.587451
2001 to 3000	1.505486	0.0850478	7.240	< 0.001	1.347692	1.681755
> 3000	1.783509	0.0957862	10.770	< 0.001	1.605315	1.981484
Dependent of Active Duty	Referent Category					
Retired	0.7982478	0.0774866	-2.320	0.020	0.6599497	0.9655273
Dependent of Retired	0.9672048	0.0234974	-1.370	0.170	0.9222299	1.014373
Active Duty	0.9571829	0.026076	-1.610	0.108	0.9074153	1.00968
5 to 12 years	Referent Category					
13 to 18 years	0.6919244	0.0166889	-15.270	< 0.001	0.6599759	0.7254195
19 to 40 years	0.7672178	0.0164675	-12.350	< 0.001	0.7356115	0.8001821
Lead Agent	0.9161343	0.0224593	-3.570	< 0.001	0.8731558	0.9612284

Consistent with the OLS and logistic models, the IRLS model also suggested a small significant increase of 0.01 visits with the use of a formal guideline use process ($p < 0.026$). Other variables significant for increased numbers of health care visits are shown

in Table 4.23. Variables with an asterisk next to the variable were associated with increased visits, while those with two asterisks were associated with decreased visits.

Figure 4.23: IRLS regression model predicting log-transformed visits in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Intervals</i>	
Cpg*	0.0119722	0.0053715	2.23	0.026	0.001444	0.0225003
Visits – before**	-0.0967374	0.0037468	-25.82	< 0.001	-0.1040811	-0.0893938
Males**	-0.011476	0.0055851	-2.05	0.040	-0.0224228	-0.0005292
Comorbidity*	0.1476169	0.0049518	29.81	< 0.001	0.1379113	0.1573224
Region 1	Referent group					
Region 2	-0.0108066	0.0102775	-1.05	0.293	-0.0309504	0.0093373
Region 3**	-0.0706506	0.0107891	-6.55	< 0.001	-0.0917973	-0.0495039
Region 4	0.0038911	0.0135071	0.29	0.773	-0.0225828	0.030365
Region 5	-0.0011495	0.0130354	-0.09	0.930	-0.0266988	0.0243998
Region 6**	-0.0709865	0.0100645	-7.05	< 0.001	-0.0907129	-0.0512601
Region 7/8**	-0.0288973	0.009956	-2.9	0.004	-0.0484111	-0.0093836
Region 9*	0.0599592	0.0116909	5.13	< 0.001	0.0370451	0.0828732
Region 10	-0.0155732	0.0188098	-0.83	0.408	-0.0524403	0.021294
Region 11**	-0.0416978	0.0141744	-2.94	0.003	-0.0694796	-0.0139159
Non-conus*	0.0394918	0.0097781	4.04	< 0.001	0.0203268	0.0586568
Multiple Facilities*	0.2955925	0.0064115	46.1	< 0.001	0.283026	0.3081591
Facility Size						
0 to 250	Referent group					
251 to 500*	0.0487748	0.0203009	2.4	0.016	0.0089851	0.0885645
501 to 1000*	0.1081721	0.0186565	5.8	< 0.001	0.0716054	0.1447387
1001 to 2000*	0.143599	0.0166532	8.62	< 0.001	0.1109588	0.1762392
2001 to 3000*	0.1624658	0.0169693	9.57	< 0.001	0.129206	0.1957256
> 3000*	0.2338926	0.0160643	14.56	< 0.001	0.2024067	0.2653785
Dependent of Active Duty	Referent group					
Retired**	-0.1096315	0.0291438	-3.76	< 0.001	-0.1667533	-0.0525098
Dependent of Retired	-0.0134657	0.0075708	-1.78	0.075	-0.0283045	0.0013731
Active Duty**	-0.0190062	0.0085094	-2.23	0.026	-0.0356846	-0.0023278
5 to 12 years	Referent group					
13 to 18 years**	-0.1346342	0.0074707	-18.02	< 0.001	-0.1492767	-0.1199916
19 to 40 years**	-0.0995747	0.0067595	-14.73	< 0.001	-0.1128234	-0.086326
Lead Agent**	-0.0389147	0.007723	-5.04	< 0.001	-0.0540518	-0.0237777
constant	0.6212012	0.0185475	33.49	< 0.001	0.5848483	0.6575542

The residuals in the above IRLS model were distributed in a reasonably normal manner as indicated by both the histogram in Figure 4.11 and the Q-Q plot in Figure 4.12.

Figure 4.11: IRLS log-transformed model: Distribution of error residuals for health care visits in the period after CPG exposure

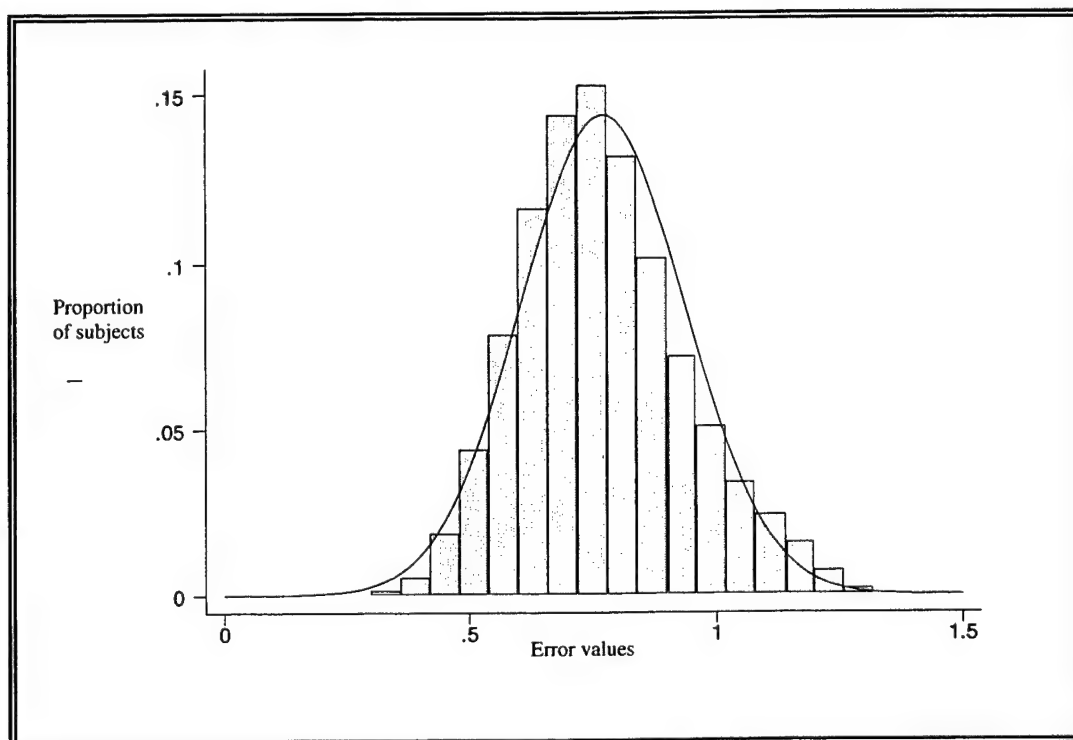
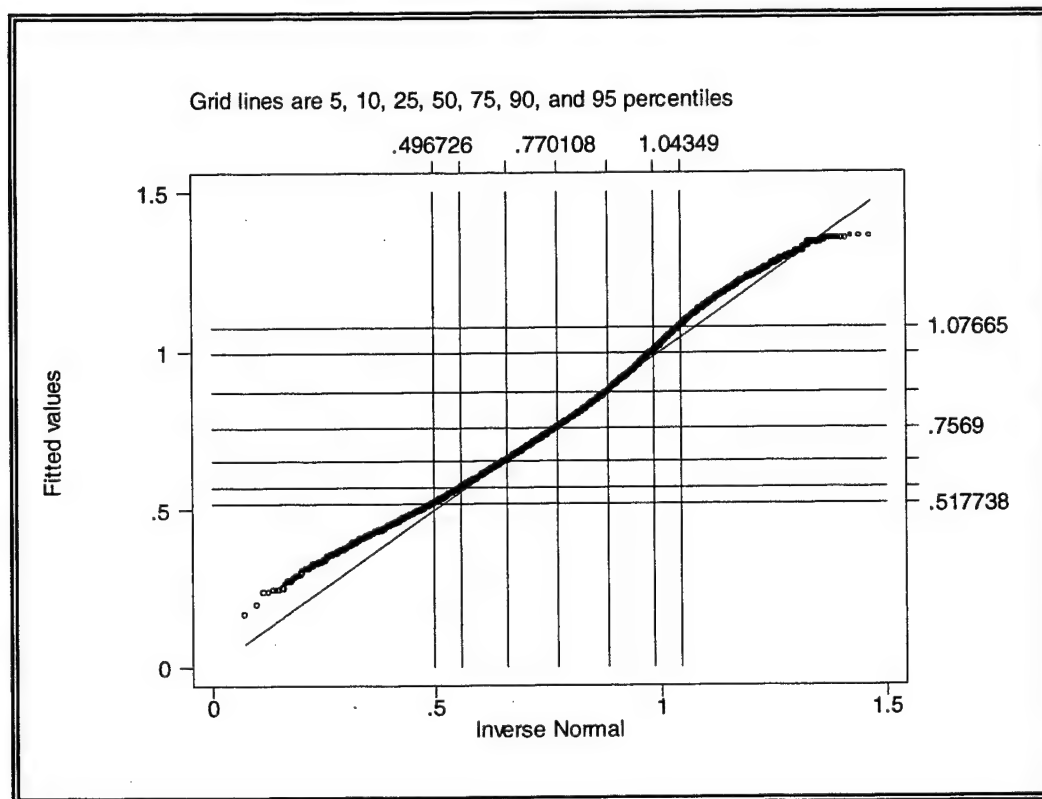


Figure 4.12: Quantile-Quantile (Q-Q) plot of residuals for log-transformed visits in period after CPG exposure using the IRLS technique



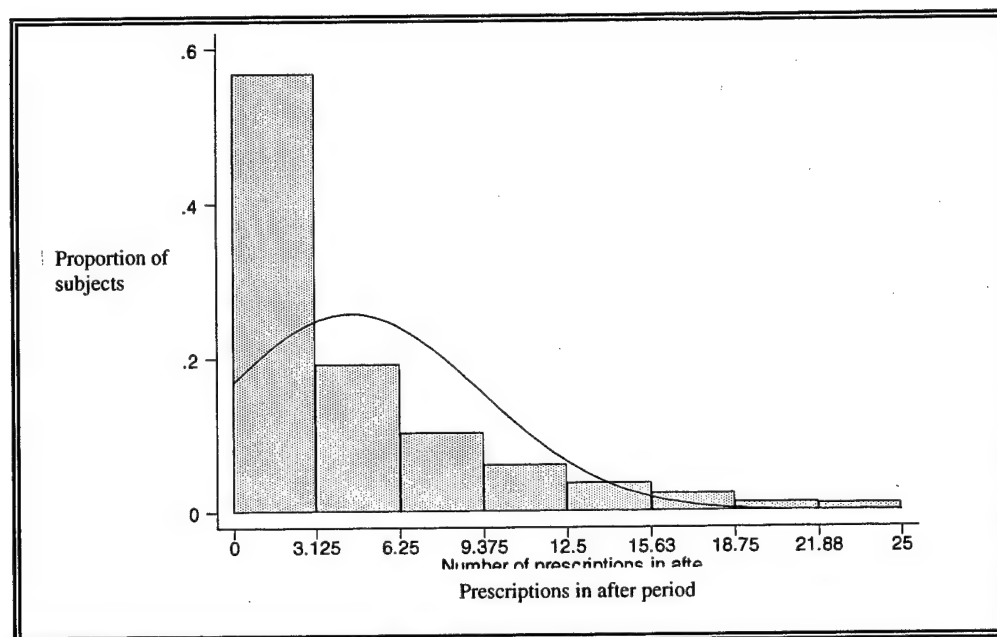
Based on the above analyses, there appears to be a significant association between the number of health care visits experienced by a subject, and the formal CPG use process. Somewhat unexpectedly however, this association suggests that CPG exposure resulted in a small increase of 0.12 visits per subject over the study time period (untransformed OLS model, $p < 0.001$). For this reason, $H_0: 3$ was rejected.

4.4.4 Prescriptions dispensed

Ho: 4: There is no difference in the period before CPG exposure, and the period after CPG exposure, in the number of prescriptions dispensed.

The distribution of the number of prescriptions dispensed to subjects being treated for asthma in the period after guideline implementation is shown in Figure 4.13. As with the other utilization data already discussed, the distribution was highly skewed to the right with most subjects getting fewer than five prescriptions. The mean number of prescriptions per subject, for the entire study period was 9.48 ± 10.11 . For the period before CPG implementation, the mean was 4.78 ± 5.66 . For the period after CPG implementation the mean was 4.70 ± 5.54 . The range of prescriptions dispensed was 0 to 123 over the course of the whole study period, 0 to 84 in the time period before CPG implementation, and 0 to 90 in the period after CPG implementation.

Figure 4.13: Distribution of prescriptions dispensed in the period after CPG exposure



The overall model was significant with an F -statistic of 1817 and a p -value less than 0.001. The R^2 and adjusted R^2 were quite high at 39.67 percent and 39.65 percent respectively, suggesting the model did a reasonably good job of explaining the factors responsible for the number of prescriptions dispensed.

The use of a formal CPG use process was not a significant predictor of the number of prescriptions dispensed to subjects treated for asthma. As seen in Table 4.24, the coefficient for the CPG variable was 0.004 ($p = 0.907$). Variables that were significantly associated with an increased number of dispensed prescriptions included: male gender ($p < 0.001$); receiving care in TRICARE regions seven/eight and nine ($p < 0.001$); receiving care in multiple facilities ($p < 0.001$); receiving care in a medium sized facility ($p =$

0.035, observations between 1001 and 2000) and being greater than 18 years of age ($p < 0.001$). Variables associated with a decreased number of dispensed prescriptions included: the presence of a comorbid respiratory condition ($p < 0.001$); receiving care in TRICARE region nine ($p = 0.003$); being on active duty status ($p < 0.001$), and being between the ages of 13 to 18 ($p < 0.001$). The results are presented in Table 4.24. The assumption of homoscedasticity, based on the Cook-Weisberg test for heteroscedasticity was not met ($p < 0.0001$).

Table 4.24: OLS regression model predicting number of prescriptions dispensed in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0041455	0.0355935	0.120	0.907	-0.0656178	0.0739087
Prescriptions - before	0.6019876	0.0029067	207.100	< 0.001	0.5962904	0.6076848
Males	0.1768483	0.0370334	4.780	< 0.001	0.1042629	0.2494337
Comorbidity	-0.5617258	0.0332693	-16.880	< 0.001	-0.6269335	-0.4965181
Region 1	Referent Group					
Region 2	0.0987109	0.0680859	1.450	0.147	-0.0347373	0.232159
Region 3	0.0526889	0.0714791	0.740	0.461	-0.08741	0.1927877
Region 4	-0.0527213	0.0894788	-0.590	0.556	-0.2280995	0.1226568
Region 5	-0.0887058	0.0863658	-1.030	0.304	-0.2579825	0.0805709
Region 6	0.011564	0.0666214	0.170	0.862	-0.1190137	0.1421417
Region 7/8	0.2109848	0.065944	3.200	< 0.001	0.0817347	0.3402349
Region 9	-0.233128	0.077468	-3.010	0.003	-0.384965	-0.0812909
Region 10	0.0443594	0.124629	0.360	0.722	-0.1999131	0.2886319
Region 11	-0.1732258	0.0939305	-1.840	0.065	-0.3573293	0.0108778
Non-conus	0.005871	0.0647755	0.090	0.928	-0.1210888	0.1328307
Multiple Facilities	0.1634945	0.0420324	3.890	< 0.001	0.0811111	0.2458779
Facility Size						
0 to 250	Referent Group					
251 to 500	0.1409953	0.134492	1.050	0.294	-0.1226086	0.4045992
501 to 1000	0.177741	0.1235945	1.440	0.150	-0.0645039	0.4199859
1001 to 2000	0.2319654	0.110318	2.100	0.035	0.0157424	0.4481884
2001 to 3000	0.1103412	0.1124145	0.980	0.326	-0.1099908	0.3306731
> 3000	0.0949249	0.1063852	0.890	0.372	-0.1135898	0.3034396
Dependent of Active Duty	Referent Group					
Retired	0.4122739	0.1931342	2.130	0.033	0.0337315	0.7908163
Dependent of Retired	0.0852481	0.0501803	1.700	0.089	-0.0131051	0.1836013
Active Duty	-0.3734533	0.05642	-6.620	< 0.001	-0.4840363	-0.2628703
5 to 12 years	Referent Group					
13 to 18 years	-0.4253517	0.049462	-8.600	< 0.001	-0.5222971	-0.3284064
19 to 40 years	0.2232027	0.0447774	4.980	< 0.001	0.1354391	0.3109662
Lead Agent	0.0008866	0.051228	0.020	0.986	-0.0995201	0.1012933
constant	1.909285	0.1221419	15.630	< 0.001	1.669887	2.148683

When the dependent and corresponding independent variables (number of prescriptions before and after CPG implementation) were log transformed, only minimal differences were observed in the model results. The overall log-transformed model was significant

with an F -statistic of 2087 ($p < 0.0001$). The R^2 and adjusted R^2 improved somewhat over the untransformed model to 43.03 and 43.01 percent respectively, however the assumption for homoscedasticity did not improve.

As seen in Table 4.25, the use of a formal CPG use process was not significant when the log-transformed number of prescriptions dispensed was the dependent variable (coefficient = 0.005, $p = 0.341$). Consistent with the previous model, male gender ($p < 0.001$), care received in TRICARE region seven and eight ($p = 0.031$), and age over 18 years ($p < 0.001$) were associated with an increased number of prescriptions dispensed. Alternately, factors consistent with the previous model for fewer number of prescriptions dispensed included the presence of a comorbid respiratory condition ($p < 0.001$), receiving care in TRICARE region nine ($p = 0.002$), being on active duty status ($p < 0.001$), or being between 13 to 18 years of age ($p < 0.001$). There were two notable differences between the log-transformed and the untransformed models. The use of multiple facilities for asthma care was no longer a significant predictor of the number of prescriptions dispensed in the log-transformed model ($p = 0.644$). Additionally, care received in TRICARE region eleven became significant as a predictor for a lower number of prescriptions dispensed in the log-transformed model ($p = 0.031$).

Table 4.25: OLS regression model predicting log-transformed number of prescriptions dispensed in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0053429	0.0056119	0.950	0.341	-0.0056564	0.0163423
Prescriptions – before	0.6319908	0.0029352	215.320	< 0.001	0.6262379	0.6377437
Males	0.0351975	0.0058398	6.030	< 0.001	0.0237516	0.0466434
Comorbidity	-0.1291625	0.005324	-24.260	< 0.001	-0.1395975	-0.1187274
Region 1	Referent Group					
Region 2	0.0245595	0.0107342	2.290	0.022	0.0035205	0.0455985
Region 3	0.0099124	0.0112694	0.880	0.379	-0.0121755	0.0320004
Region 4	-0.010244	0.0141084	-0.730	0.468	-0.0378963	0.0174084
Region 5	-0.0231402	0.0136177	-1.700	0.089	-0.0498308	0.0035504
Region 6	-0.0005804	0.0105026	-0.060	0.956	-0.0211655	0.0200048
Region 7/8	0.0223762	0.0103964	2.150	0.031	0.0019992	0.0427532
Region 9	-0.0382504	0.0122125	-3.130	0.002	-0.0621868	-0.0143139
Region 10	0.0061978	0.019647	0.320	0.752	-0.0323103	0.044706
Region 11	-0.0319975	0.0148084	-2.160	0.031	-0.061022	-0.0029731
Non-conus	-0.004944	0.010212	-0.480	0.628	-0.0249595	0.0150716
Multiple Facilities	0.0030624	0.0066208	0.460	0.644	-0.0099144	0.0160392
Facility Size						
0 to 250	Referent Group					
251 to 500	-0.0017379	0.0212036	-0.080	0.935	-0.0432969	0.0398211
501 to 1000	-0.0030227	0.0194855	-0.160	0.877	-0.0412143	0.0351689
1001 to 2000	0.0062362	0.0173925	0.360	0.720	-0.027853	0.0403254
2001 to 3000	-0.0095741	0.017723	-0.540	0.589	-0.0443112	0.025163
> 3000	-0.0031232	0.0167723	-0.190	0.852	-0.0359968	0.0297505
Dependent of Active Duty	Referent Group					
Retired	0.0584868	0.0304467	1.920	0.055	-0.0011887	0.1181623
Dependent of Retired	0.0146975	0.0079122	1.860	0.063	-0.0008104	0.0302054
Active Duty	-0.0626081	0.0088941	-7.040	< 0.001	-0.0800405	-0.0451758
5 to 12 years	Referent Group					
13 to 18 years	-0.0698834	0.0077985	-8.960	< 0.001	-0.0851684	-0.0545984
19 to 40 years	0.0162329	0.007058	2.300	0.021	0.0023991	0.0300666
Lead Agent	0.0011887	0.0080725	0.150	0.883	-0.0146334	0.0170108
constant	0.5539082	0.0196416	28.200	< 0.001	0.5154106	0.5924057

Logistic regression was also used to explore the effect of CPG use and prescriptions received. The dependent variable was dichotomized such that six or more prescriptions dispensed in the period-after CPG exposure was considered the high-prescription group

and five or less prescriptions dispensed was considered the low-prescription group. In the period before CPG exposure, the 75th percentile was seven prescriptions. Consistent with the OLS analyses, the use of CPGs in the treatment of asthma was not a significant predictor for the number of prescriptions dispensed. The goodness-of-fit test for this model was significant ($p < 0.0001$) indicating a poor fit between the data and the model. Odds ratios and related statistics are presented in Table 4.26.

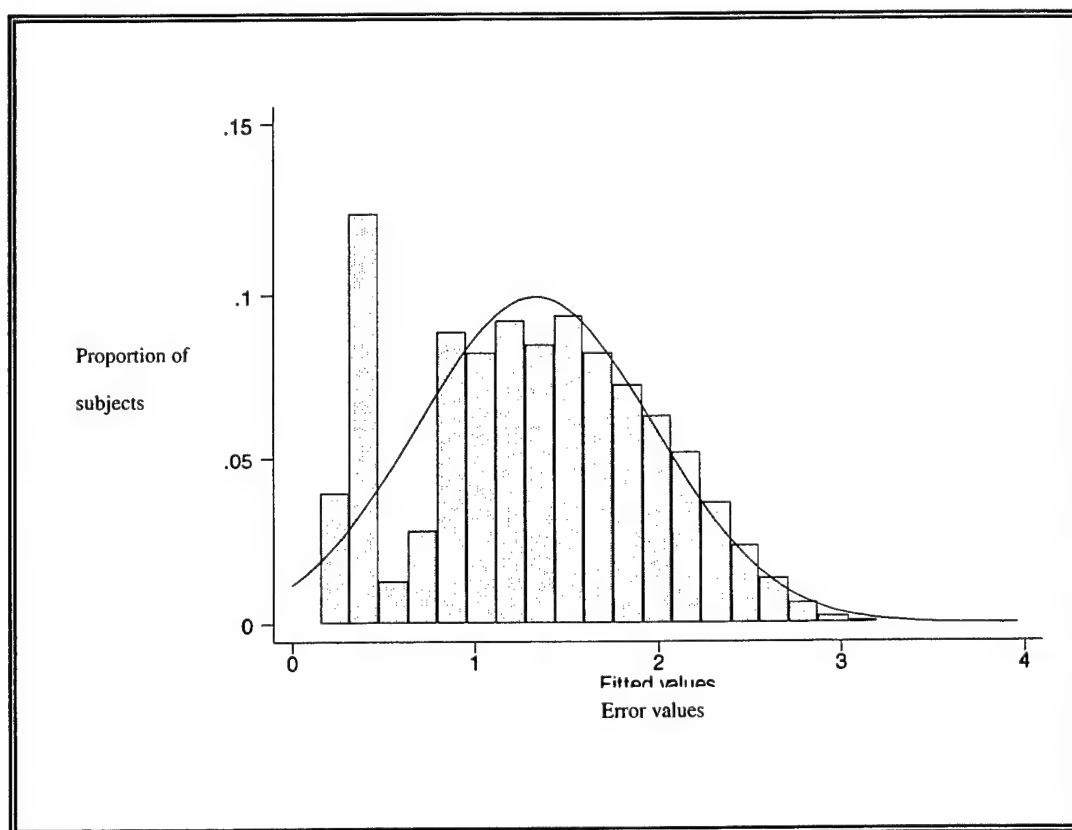
Table 4.26: Logistic regression for number of prescriptions received (high number of prescriptions ≥ 6 , low number of prescriptions ≤ 5)

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.9733063	0.0196841	-1.340	0.181	0.9354808	1.012661
Prescriptions – before	7.823209	0.1521652	105.760	< 0.001	7.530584	8.127205
Males	1.18275	0.0250453	7.930	< 0.001	1.134667	1.232871
Comorbidity	0.67784	0.0125361	-21.030	< 0.001	0.6537097	0.7028611
Region 1	Referent Group					
Region 2	1.095261	0.041835	2.380	0.017	1.01626	1.180403
Region 3	0.9778647	0.0397	-0.550	0.581	0.9030693	1.058855
Region 4	0.9476223	0.048395	-1.050	0.292	0.8573625	1.047384
Region 5	0.9234754	0.0457103	-1.610	0.108	0.8380936	1.017556
Region 6	0.98461	0.0370596	-0.410	0.680	0.9145891	1.059992
Region 7/8	1.046239	0.0390123	1.210	0.225	0.9725033	1.125565
Region 9	0.7844338	0.0355815	-5.350	< 0.001	0.7177054	0.8573662
Region 10	0.9818518	0.0692212	-0.260	0.795	0.8551369	1.127343
Region 11	0.8549951	0.0465709	-2.880	0.004	0.7684213	0.9513227
Non-conus	0.9771983	0.035926	-0.630	0.530	0.9092616	1.050211
Multiple Facilities	1.182018	0.027731	7.130	< 0.001	1.128896	1.237638
Facility Size						
0 to 250	Referent Group					
251 to 500	1.019193	0.0786218	0.250	0.805	0.8761811	1.185548
501 to 1000	0.9525293	0.068059	-0.680	0.496	0.8280552	1.095714
1001 to 2000	1.024997	0.0650105	0.390	0.697	0.9051802	1.160673
2001 to 3000	1.028127	0.0663836	0.430	0.667	0.9059132	1.166827
> 3000	0.9986445	0.0611206	-0.020	0.982	0.8857565	1.12592
Dependent of Active Duty	Referent Group					
Retired	1.318948	0.1354543	2.700	0.007	1.078476	1.61304
Dependent of Retired	1.06369	0.0300868	2.180	0.029	1.006326	1.124324
Active Duty	0.7615471	0.0247017	-8.400	< 0.001	0.7146396	0.8115336
5 to 12 years	Referent Group					
13 to 18 years	0.7928814	0.0227604	-8.080	< 0.001	0.7495035	0.8387699
19 to 40 years	1.121789	0.0285469	4.520	< 0.001	1.06721	1.179158
Lead Agent	1.078225	0.0310128	2.620	0.009	1.019122	1.140755

Use of the IRLS regression technique resulted in the use of CPGs becoming a significant predictor for prescriptions dispensed per subject ($p < 0.0001$). However, since these results were not consistent with the results of the OLS or logistic models, and since, as

observed in Figure 4.14, the distribution of the IRLS residuals did not appear to be normally distributed, the results of this model were rejected.

Figure 4.14: IRLS log-transformed model: Residuals of prescription data in the period after CPG implementation



Based on the above OLS and logistic analyses, there did not appear to be a significant association between the number of prescriptions dispensed and exposure to the formal CPG use process. For this reason, $H_0: 4$ was rejected.

4.4.5 Asthma exacerbations

Ho: 5: There is no difference in the risk of experiencing an asthma exacerbation between individuals treated before guideline implementation and those treated after guideline implementation.

As discussed previously in the methods section, an exacerbation was defined as a hospital admission with the primary diagnosis of asthma or an acute care visit with a primary diagnosis of asthma. In this study asthma exacerbations were a rare event, occurring in less than five percent of the study population. The mean (sd) number of exacerbations per subject over the course of the study period was 0.11 ± 0.56 with a range between zero and 71. For the period before CPG implementation the mean number (sd) of exacerbations per subject was 0.08 ± 0.47 with a range between zero and 71. For the period after CPG implementation the mean number (sd) of exacerbations per subject was 0.02 ± 0.24 with a range between zero and 24. With most subjects not having any exacerbations, and only 0.15 percent of the subjects (108) having more than two exacerbations, the distribution was skewed heavily to the right.

A logistic regression model was the method used to perform this analysis. The dependent variable was dichotomized by coding subjects that had experienced one or more exacerbations within the given time period as belonging to one group, and those not having experienced an exacerbation into another group. Because of the small number of

exacerbations observed in this data, individual data cell sizes of some of the independent variables became a concern. Specifically, the number of exacerbations that occurred in each TRICARE region, both before and after CPG implementation, was examined to ensure they contained an adequate number of observations. As noted in Table 4.27, with the possible exception of TRICARE region ten in the period after CPG exposure, all the cells were adequately populated.

Table 4.27: Frequency of subjects with at least one asthma exacerbation by TRICARE region for before and after CPG implementation periods

<i>TRICARE Region</i>	<i>Subjects experiencing at least one exacerbation in period before CPG Implementation</i>	<i>Subjects experiencing at least one exacerbation in period after CPG Implementation</i>
Region 1 (Northeast)	284	95
Region 2 (Mid-Atlantic)	827	344
Region 3 (Southeast)	556	129
Region 4 (Gulfsouth)	207	70
Region 5 (Heartland)	407	70
Region 6 (Southwest)	795	186
Region 7/8 (Central)	640	213
Region 9 (Southern California)	350	114
Region 10 (Golden Gate)	52	7
Region 11 (Northwest)	374	70
Region 12 (Non continental)	833	223

Other variable categories with low frequencies included the retiree category in the beneficiary variable and several of the categories describing facility size. To ensure large enough numbers of observations were available in each of the 'facility size' categories, the lower four categories were collapsed into one category, and the top two categories into another. The beneficiary variable was also regrouped into two categories – one made up of retirees and their dependents, and the other made up of active duty members

and their dependents. The resulting frequencies of these regrouped variables are presented in Table 4.28.

Table 4.28: Categorized facility size and beneficiary status variables

<i>Variable</i>	<i>Category</i>	<i>Code</i>	<i>Frequency – before period</i>	<i>Frequency – after period</i>
Facility size	0 – 2000 observations	0	495	138
	> 2000 observations	1	4830	1383
Beneficiary type	Retiree and dependents	0	874	255
	Active duty and dependents	1	4451	1266

With the exception of the substitution of these two regrouped variables for the original variables, the other independent variables for this analysis were the same as those used in the analyses of the previous dependent variables. The resulting odd ratios and related statistics are presented in Table 4.29.

Table 4.29: Logistic regression for presence or absence of an exacerbation

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Intervals</i>	
Cpg	1.220766	0.0695326	3.500	< 0.001	1.091817	1.364946
Exacerbations -before	1.045939	0.0243892	1.930	0.054	0.999213	1.09485
Males	0.9410031	0.0516434	-1.110	0.268	0.8450377	1.047867
Comorbidity	0.7100078	0.0372576	-6.530	< 0.001	0.6406139	0.7869187
Region 1	Referent group					
Region 2	2.707126	0.3237268	8.330	< 0.001	2.141505	3.42214
Region 3	1.570411	0.2148653	3.300	< 0.001	1.201022	2.05341
Region 4	1.445755	0.2334174	2.280	0.022	1.053581	1.983907
Region 5	1.103235	0.1765642	0.610	0.539	0.8061946	1.50972
Region 6	1.45008	0.1850169	2.910	0.004	1.12924	1.862076
Region 7/8	1.655377	0.2068499	4.030	< 0.001	1.295788	2.114755
Region 9	1.513621	0.2203513	2.850	0.004	1.13789	2.013419
Region 10	0.2356176	0.0933686	-3.650	< 0.001	0.1083679	0.5122889
Region 11	1.154534	0.1889782	0.880	0.380	0.8376822	1.591236
Non-conus	2.262369	0.2835527	6.510	< 0.001	1.769614	2.892333
Multiple Facilities	0.9278888	0.0641652	-1.080	0.279	0.8102775	1.062571
Facility Size > 2000	3.589807	0.3362105	13.650	< 0.001	2.987791	4.313125
Active duty and dependents	0.8062293	0.0588079	-2.950	0.003	0.6988281	0.9301367
5 to 12 years	Referent group					
13 to 18 years	0.9398368	0.0784815	-0.740	0.457	0.797944	1.106961
19 to 40 years	1.273947	0.0753696	4.090	< 0.001	1.134469	1.430574
Lead Agent	1.930555	0.1249845	10.160	< 0.001	1.700494	2.19174

These results suggested that the use of a formal CPG process in the treatment of asthma was a significant predictor of an increased number of exacerbations. Subjects who had experienced an asthma exacerbation were 1.22 times more likely to have been exposed to asthma CPG use process than subjects who had not experienced an asthma exacerbation (95% CI: 1.09 to 1.36). Other factors significantly associated with a greater risk of asthma exacerbations included care received in regions two, three, four, six, seven and eight, and nine as compared to TRICARE region two, receiving care in a larger facility, receiving care at a lead agent facility, or being in the oldest age category as compared to the youngest age category. Factors significantly associated with a lower risk of

experiencing an asthma exacerbation included the presence of a comorbid respiratory condition, being either an active duty member or dependent of an active duty member, and being between 13 and 18 years of age.

The goodness-of-fit test for this model suggested a poor fit between the data and model. Removing different combinations of variables from the model produced fluctuating goodness-of-fit results; some with better χ^2 values than others, but in no case was a combination of variables found in which the goodness-of-fit assumption was met.

Based on the above logistic analysis, there did appear to be a significant association between exposure to the CPG use process and having an exacerbation. Somewhat unexpectedly, the risk of experiencing an asthma exacerbation was significantly higher (OR = 1.22, 95% CI: 1.09, 1.36) for subjects exposed to the CPG use process as opposed to those who were not. For this reason, $H_0: 5$ was rejected.

4.4.6 Total beddays

Ho: 6: There is no difference in length of hospital stay (for a primary diagnosis of asthma) between individuals treated at MTFs before asthma guidelines were instituted, and individuals treated at MTFs after asthma guidelines were instituted.

The mean number (sd) of beddays per subject was 0.10 ± 1.08 for the entire study period, 0.06 ± 0.85 for the period before CPG exposure, and 0.04 ± 0.54 for the period after CPG

exposure. When only patients who had hospital admissions were considered, the mean number (sd) of beddays per subjects was 3.26 ± 5.2 for the entire study period, 2.05 ± 4.39 for the period prior to CPG exposure, and 1.21 ± 2.88 for the period after CPG exposure. Because of the low number of subjects with inpatient admission data in this study, the number of observations associated with several of the categorical variables was a concern. Regrouping was performed for two variables. The variables for beneficiary status and facility size were regrouped in a manner similar to the analysis of the previous dependent variable (exacerbations). An OLS model was used for this analysis, first including all subjects in the database, and then only those that had been hospitalized. For neither group was the use of a formal CPG-use process a significant predictor for asthma beddays. The results of the model including all subjects are presented in Table 4.30. In neither case was the assumption of homoscedasticity met using the Cook-Weisberg test for heteroscedasticity ($p < 0.001$).

Table 4.30: OLS regression model predicting hospital beddays in the after period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-0.0041144	0.0043334	-0.950	0.342	-0.0126079	0.004379
Beddays –before	0.1095291	0.0023674	46.270	< 0.001	0.104889	0.1141692
Males	-0.0158696	0.0041673	-3.810	< 0.001	-0.0240375	-0.007702
Comorbidity	-0.0027956	0.004073	-0.690	0.492	-0.0107787	0.0051875
Region 1	Referent category					
Region 2	-0.006306	0.0084163	-0.750	0.454	-0.0228018	0.0101899
Region 3	-0.0031123	0.0088647	-0.350	0.726	-0.0204871	0.0142625
Region 4	-0.0069243	0.0110622	-0.630	0.531	-0.0286061	0.0147575
Region 5	-0.0140423	0.0106109	-1.320	0.186	-0.0348396	0.0067551
Region 6	0.0023458	0.0082496	0.280	0.776	-0.0138235	0.018515
Region 7/8	-0.0041197	0.008161	-0.500	0.614	-0.0201153	0.0118759
Region 9	-0.008881	0.0095886	-0.930	0.354	-0.0276747	0.0099127
Region 10	-0.0266856	0.0154399	-1.730	0.084	-0.0569478	0.0035766
Region 11	-0.0352032	0.0116161	-3.030	0.002	-0.0579706	-0.012436
Non-conus	0.0156224	0.0080273	1.950	0.052	-0.0001111	0.031356
Multiple Facilities	0.0349504	0.0052075	6.710	< 0.001	0.0247437	0.0451572
Facility Size > 2000	0.012003	0.0017087	7.020	< 0.001	0.0086539	0.0153521
Active duty and dependents	-0.0076826	0.006024	-1.280	0.202	-0.0194895	0.0041244
5 to 12 years	Referent category					
13 to 18 years	0.0092459	0.0061235	1.510	0.131	-0.0027562	0.021248
19 to 40 years	0.0268384	0.0045447	5.910	< 0.001	0.0179308	0.035746
Lead Agent	0.0699827	0.0062362	11.220	< 0.001	0.0577598	0.0822056
constant	-0.0414549	0.0126508	-3.280	< 0.001	-0.0662503	-0.016659

According to this model, factors associated with an increased number of beddays included receiving care from multiple facilities, receiving care at a lead agent facility, receiving care from a large facility, or belonging to the 19 to 40 year old age group. Factors significantly associated with a decreased number of beddays included male gender and receiving care in TRICARE region eleven. Table 4.31 presents the statistics for the model utilizing only subjects with inpatient days. Of note in this model was that the presence of a comorbid respiratory condition became a significant predictor of an increased number of beddays ($p < 0.001$), whereas in the model including all subjects it

was not ($p = 0.492$). Other noteworthy observations in this model included: 1) both of the older age categories (13 to 18 years, and 19 to 40 years) were significant predictors of increased beddays ($p = 0.024$ and $p = 0.003$ respectively) compared to the five to 12 year category; and 2) care received at a facility with more than 2000 observations was no longer significantly associated with an increased number of beddays ($p=0.422$).

Table 4.31: OLS regression model predicting hospital beddays in the after period (using only inpatient subjects with one or more hospitalizations)

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-0.1293749	0.1386339	-0.930	0.351	-0.4012431	0.1424933
Beddays –before	0.0059281	0.013903	0.430	0.670	-0.0213365	0.0331926
Males	-0.126807	0.1478826	-0.860	0.391	-0.4168123	0.1631984
Comorbidity	0.3100464	0.12296	2.520	0.012	0.0689154	0.5511774
Region 1	Referent Group					
Region 2	-0.2626144	0.2661297	-0.990	0.324	-0.7845085	0.2592797
Region 3	0.1396117	0.3128186	0.450	0.655	-0.4738418	0.7530653
Region 4	-0.1919151	0.3453084	-0.560	0.578	-0.8690827	0.4852525
Region 5	0.1632361	0.3581649	0.460	0.649	-0.5391437	0.865616
Region 6	0.0779084	0.2673126	0.290	0.771	-0.4463055	0.6021223
Region 7/8	0.1857562	0.2846401	0.650	0.514	-0.3724378	0.7439503
Region 9	-0.3819353	0.3116376	-1.230	0.220	-0.9930728	0.2292022
Region 10	-0.0732235	0.4838619	-0.150	0.880	-1.022102	0.8756548
Region 11	-0.5794789	0.3416957	-1.700	0.090	-1.249562	0.090604
Non-conus	0.1870291	0.2676646	0.700	0.485	-0.337875	0.7119331
Multiple Facilities	0.2522656	0.1406761	1.790	0.073	-0.0236075	0.5281388
Facility Size > 2000	0.0952991	0.1186928	0.800	0.422	-0.1374636	0.3280617
Active duty and dependents	-0.2392606	0.187523	-1.280	0.202	-0.607003	0.1284817
5 to 12 years	Referent Group					
13 to 18 years	0.4958292	0.2197253	2.260	0.024	0.0649366	0.9267218
19 to 40 years	0.4594758	0.1563888	2.940	0.003	0.1527893	0.7661623
Lead Agent	0.7242297	0.1503003	4.820	< 0.001	0.4294832	1.018976
constant	0.1968372	0.745207	0.260	0.792	-1.264552	1.658227

This analysis also included a model in which the dependent variable for beddays in the period after CPG implementation was log-transformed. This analysis included only subjects with inpatient data. As with the other log-transformed analyses in this research, the corresponding independent variable (beddays before CPG implementation) was also log-transformed. The coefficients and statistics of this model are presented in Table 4.32.

Table 4.32: OLS regression model predicting log-transformed total beddays in the after period using only subjects with inpatient days

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-0.0262955	0.0277145	-0.950	0.343	-0.080645	0.028054
Beddays –before	-0.4778668	0.0170238	-28.070	< 0.001	-0.5112514	-0.4444823
Males	-0.0374118	0.0295738	-1.270	0.206	-0.0954076	0.0205841
Comorbidity	0.0685411	0.024578	2.790	0.005	0.0203424	0.1167398
Region 1	Referent group					
Region 2	-0.0955635	0.0532144	-1.800	0.073	-0.1999196	0.0087926
Region 3	-0.0747515	0.0625373	-1.200	0.232	-0.1973905	0.0478874
Region 4	-0.1105761	0.0690398	-1.600	0.109	-0.2459668	0.0248146
Region 5	-0.0486305	0.0716094	-0.680	0.497	-0.1890604	0.0917993
Region 6	-0.0246258	0.0534519	-0.460	0.645	-0.1294478	0.0801962
Region 7/8	-0.0121092	0.0569093	-0.210	0.832	-0.1237113	0.0994929
Region 9	-0.1609139	0.0623022	-2.580	0.010	-0.2830917	-0.038736
Region 10	-0.0018742	0.0967426	-0.020	0.985	-0.1915915	0.1878431
Region 11	-0.2004787	0.0683313	-2.930	0.003	-0.3344799	-0.0664775
Non-conus	-0.0132703	0.053513	-0.250	0.804	-0.118212	0.0916714
Multiple Facilities	0.0526456	0.0282242	1.870	0.062	-0.0027036	0.1079947
Facility Size > 2000	0.0369874	0.0237389	1.560	0.119	-0.0095658	0.0835407
Active duty and dependents	-0.0182264	0.0374882	-0.490	0.627	-0.0917427	0.05529
5 to 12 years	Referent group					
13 to 18 years	0.1612691	0.0439424	3.670	< 0.001	0.0750958	0.2474424
19 to 40 years	0.1511838	0.031281	4.830	< 0.001	0.0898402	0.2125275
Lead Agent	0.1948644	0.0300164	6.490	< 0.001	0.1360008	0.2537281
constant	0.5293691	0.1493105	3.550	< 0.001	0.2365635	0.8221748

The formal CPG-use process for delivering asthma care was non-significant in this model. As with the non-transformed model, factors significantly associated with

increased beddays were the presence of a respiratory comorbidity ($p = 0.005$), being between 13 to 18 years of age ($p < 0.001$), being between 19 to 40 years of age ($p < 0.001$), and receiving care at a lead agent facility ($p < 0.001$). Factors significantly associated with decrease number of beddays included receiving care in TRICARE regions nine ($p = 0.011$) and eleven ($p = 0.003$). The use of an IRLS model was not included in this analysis because of the failure of the residuals to form a normal distribution. Dichotomizing the dependent variable into groups of 'any' beddays and 'no' beddays and using a logistic model found that the formal CPG use process was nonsignificant as a predictor of beddays ($OR = 1.16$; 95% CI: 0.98 to 1.38). The results of the logistic model are presented in Table 4.33.

Table 4.33: Logistic regression predicting any hospital beddays

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	1.165202	0.1029135	1.730	0.083	0.9799882	1.38542
Beddays – before	5.106291	0.5717989	14.560	<0.001	4.100045	6.359493
Males	0.5731325	0.0529613	-6.020	<0.001	0.4781875	0.686929
Comorbidity	0.7048526	0.0564009	-4.370	<0.001	0.6025413	0.8245362
Region 1	Referent group					
Region 2	0.8223957	0.1384693	-1.160	0.246	0.5912367	1.143932
Region 3	0.8298439	0.1609785	-0.960	0.336	0.567381	1.213719
Region 4	0.7026166	0.1620427	-1.530	0.126	0.4471033	1.104152
Region 5	0.6403426	0.1374268	-2.080	0.038	0.4204672	0.9751976
Region 6	1.009577	0.166198	0.060	0.954	0.7311614	1.394008
Region 7/8	0.9421642	0.157813	-0.360	0.722	0.6785001	1.308288
Region 9	0.6381962	0.1300613	-2.200	0.028	0.4280392	0.9515353
Region 10	0.7715668	0.2117027	-0.950	0.345	0.4506305	1.321072
Region 11	0.4921777	0.1160752	-3.010	0.003	0.3100092	0.7813927
Non-conus	1.460117	0.2376345	2.330	0.020	1.061339	2.008727
Multiple Facilitateis	1.671812	0.1404757	6.120	<0.001	1.417961	1.971109
Facility Size > 2000	5.170546	0.9089786	9.350	<0.001	3.663496	7.29755
Active duty and dependents	0.8582986	0.1042909	-1.260	0.209	0.6764097	1.089098
5 to 12 years	Referent group					
13 to 18 years	1.601887	0.2264984	3.330	0.001	1.214161	2.113427
19 to 40 years	2.835443	0.2830882	10.440	<0.001	2.331512	3.448292
Lead Agent	3.128998	0.2957789	12.070	<0.001	2.599816	3.765892

Based on the above OLS and logistic analyses, there does not appear to be a significant association between CPG exposure and the number of beddays for asthma related hospital admissions. For this reason, $H_0: 6$ was not rejected.

4.4.7 Long-term control medications

Ho: 7: The proportion of asthma patients treated with long-term control (LTC) medications does not differ before the and after the institution of asthma guidelines.

The proportion of subjects using LTCs increased significantly for both groups between the before and after periods of this study. For those in the group exposed to the CPG use process, the proportion of subjects using LTC medications increased from 0.30 to 0.66 ($\chi^2 = 6480$, $df = 2$, $p < 0.001$). For subjects in the group not exposed to the formal CPG use program, the proportion of subjects using LTC medications increased from 0.30 to 0.65 ($\chi^2 = 10251$, $df = 2$, $p < 0.001$). Combined, the proportion of subjects using LTC medications increased from 0.30 to 0.65 ($\chi^2 = 37878$, $df = 2$, $p < 0.001$). Table 4.34 presents the frequencies of each group.

Table 4.34 Distribution of long-term controller medication use by group and period:

<i>Group tested</i>	<i>Concordant (LTC used in both periods)</i>	<i>Concordant (No use of LTC in either period)</i>	<i>Discordant (LTC only in before period)</i>	<i>Discordant (LTC only in after period)</i>	<i>McNemar Chi-Square (df=2)</i>	<i>p-value</i>
Both Groups	15305	18707	6351	31527	37878	< 0.001
Control group	5911	6945	2563	12417	6480	< 0.001
Control group	9394	11762	3788	1911	10251	< 0.001

A two-sample test of proportions was used to determine if the proportion of subjects using long-term controller medications in the period after CPG exposure was similar between the CPG use group and the no-CPG use group. In this test, the hypothesis was that the two proportions were the same. As noted in the results presented in Table 4.35, a significant difference in proportions was observed between the two groups, with the group exposed to CPGs having a higher proportion of long-term controller medication use than the group not exposed to the CPG-use process.

Table 4.35 Two-sample test of proportions comparing long-term controller medication use in the CPG and control groups in the period after CPG implementation.

<i>Variable</i>	<i>Mean</i>	<i>Std. Err.</i>	<i>Z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
CPG use	.6584279	.0028424	231.641	< 0.0001	.6528568	.663999
No CPG use	.6470241	.0022769	284.171	< 0.0001	.6425615	.6514867
diff	.0114038	.0036419			.0042658	.0185419
	under Ho:	.0036485	3.12562	0.0018		
Ho: proportion(CPG use) - proportion(No CPG use) = diff = 0 Ha: diff \neq 0 z = 3.126 P > z = 0.0018						
CPG use group:	Number of obs = 27836					
No-CPG use group:	Number of obs = 44054					

The mean number of long-term controller prescriptions dispensed per subject also increased between the 'before' and 'after' periods for both the CPG-use group ($p < 0.001$) and control group ($p < 0.001$). For those in the CPG use group, the average number of long-term controller prescriptions increased from 0.827 ± 1.83 in the time period before CPG implementation to 2.457 ± 3.34 in the period after for a mean change of 1.63 ± 3.76 prescriptions. For those in the no CPG-use group, the average number of long-term controller prescriptions increased from 0.801 ± 1.78 to 2.5 ± 3.44 for a mean change of 1.7 ± 3.78 prescriptions. Although the difference in the mean change in long-term controller medications dispensed was significantly different between the CPG group and the control ($t = -2.42$, $p = 0.015$), it is unlikely that the a difference of one percent (0.65 versus 0.64) represents a clinically significant difference.

The results of these analyses suggested that the proportion of subjects that were dispensed long-term controller medications increased significantly over time. The magnitude of change in this proportion, although significantly different between the exposed and non-exposed groups, was not likely to be of clinical significance. Because the improvement in the change in the proportion of long-term inhalers was similar between the CPG-use group and the group not using CPGs, H_0 7 could not be rejected.

4.4.8 Comorbidity

Up to this point, the comorbidity variable used in all analyses was defined as the presence or absence of any respiratory comorbidity, regardless of whether the comorbidity was chronic or acute. Because of the concern that many acute respiratory conditions are not relevant to the pathogenesis of asthma, another comorbidity variable was created that only included the chronic conditions of sinusitis, bronchitis, and COPD. Selective OLS and logistic models were then re-evaluated for each of the outcome variables with the modified comorbidity variable. Very little effect was observed on the outcome variables as a consequence of redefining the comorbidity variable. The cost savings predicted for the CPG-use group remained significant ($p = 0.021$) and varied by only \$0.04 between models (-\$55.61 versus -\$55.65). The effect on total encounters remained non-significant, as did the total numbers of beddays and prescriptions. Total number of visits (0.107, $p < 0.001$) and exacerbations (OR = 1.20; CI: 1.07 to 1.34) remained significantly higher for those in the CPG-use group compared to the control. Of particular note

however, was that when the modified comorbidity variable was used in the model, the cost associated with a comorbid disease increased as expected (\$209.30, $p = 0.003$), whereas in the previous models it did not ($-\$6.67$, $p = 0.764$). The results of these models are presented in Appendix H.

4.4.9 Inpatient/Outpatient Sub-analyses

To further investigate the apparent paradox between clinical and economic outcomes that occurred with the CPG-use process, two sub-analyses were conducted. First, the risk of experiencing an acute care or an inpatient visit was determined based on CPG-use; and second, the cost associated with an inpatient and outpatient visit was determined based upon CPG-use exposure.

Logistic regression models, using all subjects with observations in the before and after groups, were used to determine the odds that a subject would experience an acute care visit (including emergency room visits) or an inpatient visit as a result of being exposed to the CPG-use process. As noted in Table 4.36, the odds of experiencing an acute care visit were significantly higher for subjects exposed to the CPG-use process as compared to subjects with no exposure (OR = 1.15; 95% CI: 1.11 to 1.19). This result was opposite of what would be expected if asthma treatment was improved through the use of the formal CPG-use process. Of further interest, as shown in Table 4.36, was the increased risk in the before period, as compared to the after period, of a subject experiencing an acute care visit (OR = 1.30; 95%CI 1.26 to 1.34). This was consistent with the results of

previous analyses in this research that found that there was a decrease in patient visits between the before and after periods.

Table 4.36: Logistic regression prediciting the odds of experiencing an acute care visit if exposed to the CPG-use process.

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	1.1522	0.0208	7.860	<0.001	1.1123	1.1937
Acute care visits - before	1.3016	0.0216	15.870	<0.001	1.2599	1.3447
Males	1.0404	0.0207	1.990	0.047	1.0005	1.0818
Comorbidity	0.8392	0.0152	-9.690	<0.001	0.8100	0.8695
Region 1	Referent					
Region 2	2.0248	0.0803	17.790	<0.001	1.8734	2.1885
Region 3	1.7992	0.0752	14.050	<0.001	1.6577	1.9528
Region 4	1.2634	0.0679	4.350	<0.001	1.1371	1.4037
Region 5	1.6838	0.0763	11.500	<0.001	1.5407	1.8401
Region 6	1.3553	0.0558	7.380	<0.001	1.2502	1.4693
Region 7/8	1.6698	0.0666	12.860	<0.001	1.5443	1.8055
Region 9	1.0894	0.0535	1.740	0.081	0.9894	1.1995
Region 10	0.5023	0.0508	-6.810	<0.001	0.4121	0.6124
Region 11	1.5061	0.0778	7.930	<0.001	1.3611	1.6664
Non-conus	2.1903	0.0859	20.000	<0.001	2.0283	2.3653
Multiple Facilities	2.4308	0.0535	40.350	<0.001	2.3282	2.5380
Facility size > 2000	2.3300	0.0558	35.330	<0.001	2.2232	2.4419
Active duty/dependents	1.4138	0.0385	12.720	<0.001	1.3403	1.4913
5 to 12 years	Referent					
13 to 18 years	0.9317	0.0251	-2.620	0.009	0.8838	0.9823
19 to 40 years	1.1253	0.0258	5.150	<0.001	1.0759	1.1770
Lead Agent	1.4815	0.0353	16.510	<0.001	1.4139	1.5522

If the CPG-use process was effective in improving asthma therapy, it would be expected that there would be fewer hospital visits in the after period than in the before period.

Exposure to the CPG-use process had no significant effect on the risk of an asthma

subject experiencing an inpatient visit (OR = 0.998; 95% CI: 0.77 to 1.28). However, as noted in Table 4.37, the risk of an inpatient hospital admission was more than six times greater in the before period than the after period. This is consistent with previous findings in this research.

Table 4.37: Logistic regression predicting the odds of experiencing an inpatient visit if exposed to the CPG-use process.

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std error</i>	<i>z</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.9979	0.1264	-0.020	0.987	0.7785	1.2792
Inpatient visits - before	6.5503	0.9427	13.060	<0.001	4.9404	8.6847
Males	1.0709	0.1362	0.540	0.590	0.8347	1.3740
Comorbidity	0.4988	0.0577	-6.010	<0.001	0.3976	0.6258
Region 1	Referent					
Region 2	1.2431	0.3003	0.900	0.368	0.7743	1.9957
Region 3	1.0682	0.2868	0.250	0.806	0.6311	1.8079
Region 4	0.9830	0.3186	-0.050	0.958	0.5208	1.8553
Region 5	0.5614	0.1967	-1.650	0.099	0.2825	1.1154
Region 6	1.0736	0.2634	0.290	0.772	0.6637	1.7365
Region 7/8	1.2070	0.2968	0.770	0.444	0.7455	1.9543
Region 9	0.6660	0.2027	-1.340	0.182	0.3668	1.2093
Region 10	0.1865	0.1382	-2.270	0.023	0.0436	0.7973
Region 11	0.4358	0.1713	-2.110	0.035	0.2017	0.9417
Non-conus	1.4865	0.3678	1.600	0.109	0.9153	2.4141
Multiple Facilities	2.3763	0.3259	6.310	<0.001	1.8162	3.1091
Facility size > 2000	2.2291	0.4024	4.440	<0.001	1.5648	3.1755
Active duty/dependents	1.0591	0.2046	0.300	0.766	0.7252	1.5466
5 to 12 years	Referent					
13 to 18 years	0.7846	0.1328	-1.430	0.152	0.5631	1.0932
19 to 40 years	0.6208	0.1000	-2.960	0.003	0.4528	0.8511
Lead Agent	3.1244	0.4266	8.340	<0.001	2.3908	4.0832

The second sub-analysis consisted of comparing inpatient and outpatient cost based on exposure to the CPG-use process. Since the previous analysis suggested no difference in the number of visits that occurred between the CPG group and the control, this analysis was done to determine if the intensity of the visits were different. A higher cost per visit might suggest a sicker patient, which in turn might reflect a higher cost. It would be expected that if the CPG-use process improved asthma therapy, that the subsequent therapy would be associated with less cost. As seen in Table 4.38, the results of a bivariate analysis between the before and after groups of the inpatient and outpatient cohorts were consistent with the results of the previous analyses in this research. There was a significant decrease in cost for both cohorts in both the exposed and non-exposed groups.

Table 4.38: Cost comparison for inpatient and outpatient cohorts

<i>Inpatient Cohorts</i>				<i>Outpatient Cohorts (</i>		
Before	CPG (n = 939)	No-CPG (n = 1266)	p-value	CPG (n = 26897)	No-CPG (n = 42788)	p-value
	x = \$6169 sd = \$20879 obs = 939	x = \$6775 sd = \$20257 obs = 1266	0.49	x = \$453 sd = \$661 obs = 26897	x = \$452 sd = \$657 obs = 42788	0.90
After	x = \$3859 sd = \$12026 obs = 939	x = \$5132 sd = \$19550 obs = 1266	0.08	x = \$411 sd = \$696 obs = 26897	x = \$410 sd = \$707 obs = 42788	0.81
p-value	0.003	0.038		< 0.001	< 0.001	

x = cost mean, sd = standard deviation, obs = number of observations

When adjusting for covariates, the effect of CPG on costs for the inpatient cohort was \$1632.06 ($p = 0.038$). As noted in Table 4.39, none of the clinical outcomes for the inpatient cohort were statistically significant. When only the outpatient cohort was

considered there was no significant change in cost for the CPG-use group (-\$9.57, $p = 0.93$), however health care visits increased significantly (0.129, $p < 0.001$) as did the number of exacerbations (OR = 1.24; 95% CI: 1.10 to 1.40). These results are presented in Table 4.39.

Table 4.39: Comparison of outcomes based on inpatient, outpatient, or combined analyses using OLS and/or logistic modeling techniques

<i>Dependent Variable</i>	<i>Model Iteration</i>	<i>Coefficient</i>	<i>Odds Ratio</i>	<i>Std Error</i>	<i>t-value</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Costs	All Patients	-\$55.65	N/A	24.07	-2.31	N/A	0.021	-102.84	-8.46
	Inpatient cohort	-\$1632.06	N/A	785.60	-2.08	N/A	0.038	-3172.67	-91.45
	Outpatient cohort	-\$9.57	N/A	5.69	-1.68	N/A	0.093	-20.73	-1.593
Encounters (OLS)	All Patients	0.071	N/A	0.05	1.47	N/A	0.143	-0.0240	0.1668
	Inpatient cohort	-0.422	N/A	0.46	-0.92	N/A	0.36	-1.325	0.481
	Outpatient cohort	0.087	N/A	0.048	1.82	N/A	0.069	-0.007	0.181
Visits (OLS)	All Patients	0.122	N/A	0.0235	5.21	N/A	<0.001	0.0762	0.168
	Inpatient cohort	-0.034	N/A	0.222	-0.15	N/A	0.877	-0.469	0.401
	Outpatient cohort	0.129	N/A	0.023	5.55	N/A	<0.001	0.083	0.174
Prescriptions (OLS)	All Patients	0.004	N/A	0.035	0.12	N/A	0.907	-0.065	0.074
	Inpatient cohort	-0.301	N/A	0.317	-0.95	N/A	0.343	-0.923	0.321
	Outpatient cohort	0.012	N/A	0.035	0.33	N/A	0.740	-0.057	0.081
Exacerbations (Logistic)	All Patients	N/A	1.22	0.0695	N/A	3.50	<0.001	1.0918	1.3649
	Inpatient cohort	N/A	1.12	0.178	N/A	0.72	0.474	0.820	1.532
	Outpatient cohort	N/A	1.24	0.077	N/A	3.54	<0.001	1.102	1.404
Beddays (OLS)	All patients	-0.004	N/A	0.004	-0.95	N/A	0.342	-0.0126	0.0044
	Inpatient cohort	-0.148	N/A	0.140	-1.06	N/A	0.288	-0.423	0.126
	Outpatient cohort	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

4.4.10 Service Type Sub-analyses

Another potential explanation for the paradox noted above between the economic and clinical outcome findings of this research are inter-service differences in the way health care is delivered. To evaluate this, the CPG variable was replaced with a categorical

variable representing service type. The Army was used as the referent group. The effects of each service on the outcomes are presented in Table 4.40. Interestingly, when partitioned by service type, the earlier cost savings observed for the Army as compared to the combined control group, was no longer significant. Differences in effects, however, were noted between the Air Force and Navy in respect to four of the five clinical outcomes evaluated. Compared to the Army, subjects treated at Air Force facilities experienced a significant decrease in beddays, exacerbations, and visits and a significant increase in prescriptions dispensed. For the Navy, only a significant increase in number of exacerbations, as compared to the Army, were observed.

Table 4.40: Evaluation of asthma outcomes by military service type

<i>Variable</i>	<i>Service</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cost	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	35.9584	29.4558	1.22	0.22	-21.7748	93.6918
	Air Force	32.4321	27.9124	1.16	0.245	-22.276	87.1402
Health care encounters	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	-0.0716	0.0596	-1.2	0.229	-0.1884	0.0451
	Air Force	-0.0031	0.0564	-0.05	0.957	-0.1137	0.1075
Health care visits	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	-0.0342	0.0287	-1.19	0.234	-0.0905	0.0221
	Air Force	-0.1212	0.0272	-4.45	<0.001	-0.1745	-0.0678
Prescriptions	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	-0.0835	0.0435	-1.92	0.055	-0.1688	0.0018
	Air Force	0.0833	0.0412	2.02	0.043	0.0025	0.1642
Exacerbations	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	0.0053	0.002	2.6	0.009	0.0013	0.0093
	Air Force	-0.0043	0.0019	-2.28	0.023	-0.0081	0.0006
Beddays	Army	Referent	Referent	Referent	Referent	Referent	Referent
	Navy	0.0091	0.0054	1.69	0.09	-0.0014	0.0197
	Air Force	-0.0118	0.005	-2.33	0.02	-0.0216	-0.0019

To further investigate the possibility of service differences between the Navy and Air Force, the mean change in outcomes between time periods were calculated and compared using t-tests. As illustrated in Table 4.41, significant differences were observed between Air Force and Navy in the change that occurred in three outcomes (encounters, visits, and exacerbations), while in three other outcomes (cost, prescriptions dispensed, and beddays), the change was not significant.

Table 4.41: Comparison of cost and utilization between Navy and Air Force services

<i>Variable</i>	<i>Service</i>	<i>Mean Change</i>	<i>Standard Deviation</i>	<i>t-value</i>	<i>p-value</i>
Cost	Navy	-93.810	4109.23		
	Air Force	-73.610	3721.79	-0.540	0.589
Encounters	Navy	-0.403	6.90		
	Air Force	-0.711	6.88	4.670	< 0.001
Visits	Navy	-0.280	3.62		
	Air Force	-0.648	3.60	10.660	<0.001
Prescriptions	Navy	-0.123	4.76		
	Air Force	-0.063	4.81	-1.310	0.189
Exacerbations	Navy	-0.064	0.64		
	Air Force	-0.042	0.33	-4.469	<0.001
Beddays	Navy	-0.318	1.15		
	Air Force	-0.022	0.70	0.040	0.963

Chapter 5

Discussion, Conclusion and Recommendations

5.1 Introduction

This research examined the effect of clinical practice guidelines upon the clinical and economic outcomes of subjects treated for asthma within the MHS of the DoD. The results were presented in Chapter 4. This chapter presents a discussion of the results from this analysis, conclusions drawn from the results, and recommendations based on the results of this research.

As discussed in the first two chapters, asthma continues to be a major health care concern, not only from a global and national perspective, but also for the DoD. The upward trend in asthma prevalence continues to be worrisome, as do the less than optimal economic and clinical outcomes associated with current treatment strategies.(19, 22, 25)

Within the military health system of the DoD, considerable effort has been expended in the development of guidelines and in attempts to institutionalize the standards of these guidelines into everyday medical practice.(13, 158, 193) The Army, in cooperation with the RAND Corporation, has taken the lead in this effort by developing a formal guideline use process; and a schedule for department wide implementation of clinical practice guidelines for specific disease states.(14) The formal clinical practice guideline process for asthma was disseminated to Army facilities in September of 2000.

The objective of this research was to test the theory that asthma outcomes could be improved through standardizing asthma care according to recommendations provided by clinical practice guidelines. Specifically, the CPG-use process employed by the Army was evaluated for its effects on asthma outcomes. Outcomes were compared within the Army through the use of a historical control group, and between other services by way of an internal control group.

The majority of prior research suggests that economic and clinical outcomes of asthma therapy are improved when CPG recommendations are followed.(183-186) In one study, asthma outcomes did not improve with CPG implementation.(187) The primary methodology used in the above studies was the before-after design. As discussed in Chapter 2, the before-after design utilizes an external control group. This is sometimes referred to as a historical control because it is composed of subjects that come from a different time period than the group that it is being compared to.(210) The primary criticism of the before and after design is that it is sometimes difficult to differentiate between the effect of interest and effects caused by other factors occurring within the same time period.(171)

The main advantage of the research conducted for this dissertation was that in addition to a historical control, the study design included an internal control group that was composed of subjects followed over the same period of time as the subjects exposed to the CPG-use process. This permitted conclusions regarding the association between the

CPG-use process and asthma outcomes to be made while taking into consideration the effect of other factors and exposures that could have occurred over the course of the study period.(123)

The outcomes that were evaluated included: 1) cost of therapy, 2) total health care encounters, 3) total health care visits, 4) number of prescriptions dispensed, 5) number of asthma exacerbations, 5) number of asthma related inpatient beddays, and 6) proportion of long term controllers dispensed.

5.2 Discussion

At first glance, the results of this research would seem to contain a paradox: the analysis found significant decreases in cost in the group exposed to the CPG-use process, whereas for the clinical outcomes evaluated, there was either no change or the outcomes worsened. It would be expected that an intervention that decreased the cost of treating a disease would be accompanied by a corresponding improvement in at least one clinical outcome.

5.2.1 Primary findings: $H_0:1$

The first hypothesis theorized that the use of CPG recommendations made no difference on the direct costs associated with a subjects asthma therapy. The major economic finding related to this hypothesis was that the cost of treating asthma subjects decreased significantly between the periods before and after CPG implementation; and that after

controlling for other factors, this decrease was significantly different between the CPG-use group and the control group. As noted in Table 5.1, using the untransformed OLS model to predict cost, a little over $\$55 \pm \25 ($p = 0.021$) was associated with exposure to the CPG-use process. Based on the number of subjects in this study, use of the CPG process might result in an annual savings to the DoD of \$5,271,933. If generalized to include the all asthmatics (paired and non-paired) in the DoD population, the savings increase to over \$15 million annually. The range of savings, based on the 95 percent confidence intervals, is estimated to be between \$2.5 million and \$30 million.

Because the assumption for homoskedasticity was not met, these results must be interpreted with caution. It should be noted however, that the overall direction of the cost-savings, and the significance of the model were confirmed using several different model iterations. These results are illustrated in Table 5.1.

Table 5.1: Comparison of the results of various regression techniques for each of the outcome variables.

<i>Dependent Variable</i>	<i>Model Iteration</i>	<i>CPG Coefficient t</i>	<i>Odds Ratio</i>	<i>Std Error</i>	<i>t or z value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Costs	OLS - untransformed	-55.6534	N/A	24.0756	-2.31	0.021	-102.8414	-8.4653
	OLS - log-transformed	-0.0612	N/A	0.0140	-4.36	<0.001	-0.0886	-0.0337
	OLS - log-transformed*	-0.0321	N/A	0.0141	-2.27	0.023	-0.0599	-0.0044
	IRLS - log-transformed	-0.0578	N/A	0.0135	-4.28	<0.001	-0.0842	-0.0313
Encounters	OLS - untransformed	0.0714	N/A	0.0487	1.47	0.143	-0.0240	0.1668
	OLS - log-transformed	0.0034	N/A	0.0056	0.61	0.540	-0.0075	0.0144
	IRLS - log-transformed	0.0030	N/A	0.0058	0.52	0.606	-0.0084	0.0144
	Logistic		0.98	0.0201	-0.61	0.542	0.9489	1.0279
Visits	OLS - untransformed	0.1222	N/A	0.0235	5.21	<0.001	0.0762	0.1682
	OLS - log-transformed	0.0204	N/A	0.0054	3.77	<0.001	0.0098	0.0310
	IRLS - log-transformed	0.0120	N/A	0.0054	2.23	0.026	0.0014	0.0225
	Logistic		1.04	0.0179	2.66	0.008	1.0120	1.0822
Prescriptions	OLS - untransformed	0.0041	N/A	0.0356	0.12	0.907	-0.0656	0.0739
	OLS - log-transformed	0.0053	N/A	0.00561	0.95	0.341	-0.0057	0.0163
	Logistic		0.97	0.01968	-1.34	0.181	0.9355	1.0127
Exacerbations	Logistic		1.22	0.0695	N/A	<0.001	1.0918	1.3649
Beddays	OLS - untransformed	-0.0041	N/A	0.0043	-0.95	0.342	-0.0126	0.0044
	OLS - untransformed**	-0.1294	N/A	0.1386	-0.93	0.351	-0.4012	0.1425
	OLS -log-transformed**	-0.0263	N/A	0.0277	-0.95	0.343	-0.0806	0.0281
	Logistic		1.17	0.1029	1.73	0.083	0.9800	1.3854

* Model dropped three variables (multiple facilities, lead agent, and comorbid conditions)

** Model includes only inpatients

That the use of CPG recommendations in asthma therapy results in cost-savings, appears to be consistent with the results of most other researchers. In one study Kelly reported a decrease of \$1145 per subject after CPG implementation ($p < 0.001$), and in another, Wazeka and associates reported a decrease in hospital charges of 26% (\$9,329.53 to a mean of \$6,875.90, $p < 0.001$) with the implementation of CPGs.(185, 186) On the other

hand, Kwan-Gett et al reported no change in total costs one year before and after the implementation of an inpatient asthma clinical pathway.(187)

5.2.2 Primary findings: H₀:2 through H₀:6

Clinical outcomes were addressed in hypothesis two through hypothesis six. In each case, the null hypothesis was that formal CPG implementation would have no effect on the outcome. The findings of this research, in regards to health care encounters (H₀:2), health care visits (H₀:3), asthma exacerbations (H₀:4), prescriptions dispensed (H₀:5), and asthma related beddays (H₀:6) are discussed below.

As already mentioned, to correspond with a significant improvement in economic outcomes, it would be reasonable to expect an accompanying improvement in at least one of the clinical outcomes. This was the case in most of the previous studies reviewed that used a before-after research design. Wazeka et al reported a decrease in length of hospital stay from 4.2 days per subject before CPGs to 2.7 days after ($p < 0.0001$). (185) Akerman and associates reported a significant reduction in asthma relapse rates as well as admission rates after the implementation of CPGs. After intervention, mean monthly asthma relapse rates dropped from 12.3 percent to 7.83 percent ($p < 0.001$). The asthma admission rate decreased from 4.83 to 3.90 per 100 emergency department visits ($p < 0.05$). (184) Based on observed changes in intermediate indicators, Emond and associates concluded that CPG use resulted in improved outcomes for asthmatic subjects. Twenty percent of patients before CPG implementation, as compared to over 80 percent after, had

an initial peak-flow (PF) measurement obtained upon admission ($p < 0.001$). Follow-up PF readings improved in a similar manner. From a low of 22 percent of subjects in the baseline period, PF measurements increased to 70 percent, 78 percent, and 62 percent in the months following CPG intervention ($p < 0.001$). Another intermediate indicator that improved was the time between hospital admission and receipt of pharmacologic therapy. The mean delay to receive β -agonist therapy was reduced by 16 minutes ($p < 0.001$) while the mean delay to receive steroid therapy was reduced by 34 minutes ($p < 0.04$). The two outcome measures reported in this study also improved. The mean emergency department length of stay decreased by 58 minutes ($p = 0.01$) and inpatient admission decreased ($p = 0.05$).⁽¹⁸³⁾

Kelly and associates also reported the improvement in asthma outcomes after the implementation of CPGs. Length of stay was significantly lower in the CPG group compared with the control group (36 hours versus 71 hours, $p < 0.001$). It was also determined that subjects in the CPG group were more likely than the control group to complete asthma teaching while hospitalized (65 % versus 18 %, $p < 0.001$), to be discharged with a prescription for a controller medication (88 % versus 53 %, $p < 0.01$), and to have a peak flow meter (57 % versus 23 %, $p < 0.05$), and a spacer device (100 % versus 71 %, $p < 0.001$) for home use.⁽¹⁸⁶⁾ In a comparison of resources and outcomes before and after asthma CPG implementation, Kwann-Gett and associates found a significant change in laboratory charges (\$26 versus \$39, $p < 0.05$) and radiology charges (\$32 versus \$55, $p < 0.001$), however no significant differences were observed in the use

of steroids or peak flowmeters, average lengths of stay, or total charges between the groups.(187)

Taking into consideration the historical component of this research, the results closely mirrored those of the studies discussed above in regards to clinical outcomes. Not only did the economic outcomes in the CPG-use group improve between the before and after periods, but also, significant improvements in each of the clinical outcomes were noted over the same period. Total health care encounters decreased by just over a half an encounter per subject in the nine month period ($p < 0.001$), total visits decreased by just over a half a visit per subject ($p < 0.001$), inpatient days decreased by 0.03 days per subject ($p < 0.001$), and the number of exacerbations decreased by 0.07 per subject ($p < 0.001$). Although the mean number of prescriptions dispensed per subject also decreased between time periods, the decrease was not significant ($p = 0.08$).

Upon inclusion of the internal control group into the analyses however, different conclusions regarding the clinical outcomes were reached from those stated above. This was true for the comparison across groups with t-tests, as well for the results obtained through regression models.

No significant differences were observed in the amount of change for clinical outcomes when comparisons with t-tests were made between subjects exposed, and not exposed, to the CPG-use process ($p > 0.05$ for all outcomes). When regression techniques were used

to adjust for the effects of gender, presence of a comorbid respiratory condition, TRICARE region, care received at multiple facilities, size of facility, beneficiary category, care received within a lead agent facility, and age, several significant differences were noted in the clinical outcomes between the subjects of the exposed, and not-exposed groups. These included total health care visits and number of exacerbations.

As mentioned earlier, because the formal CPG-use process was associated with a significant decrease in asthma cost ($-\$55 \pm 25$, $p = 0.021$), it was expected that a corresponding improvement in at least one of the clinical outcomes would be observed. This did not happen. In fact, the association between the CPG-use process and two of the outcomes of interest, was in the opposite direction of what was expected. Albeit small, subjects with an asthma exacerbation had an increased risk of being exposed to the CPG-use process ($OR = 1.22$, $p < 0.001$). Additionally, those exposed to the CPG use process had an average increase of 0.122 ($p < 0.001$) more visits than those not exposed. There was no significant difference in the total number of health care encounters, the total number of prescriptions dispensed, or the total number of asthma related beddays, between the exposed and non-exposed subjects.

5.2.3 Association between Economic and Clinical Outcomes

There are at least three ways to explain this paradox between improvements observed in the economic outcome, and lack of improvement in clinical outcomes. The first involves possible additive effects that occur when evaluating multiple non-significant factors, the

second has to do with the internal validity of the CPG-use process as the intervention for evaluating the effect of CPGs on asthma outcomes, and the third has to do with the effects of factors, other than the CPG-use process, on the outcomes evaluated.

In this research, the economic effect of the CPG-use process was measured by one outcome – total cost. On the other hand, the clinical effect of the CPG process was evaluated by five outcomes. Three of the five outcomes had a small non-significant improvement in the expected direction in at least one of the models evaluated. Two of the outcomes showed small significant improvements in outcomes for the control group. It may be possible that the combination of a number of small non-significant effects on the clinical outcomes could have resulted in an overall significant effect on the economic outcome.

Internal validity issues, specifically those of selection bias, may also have been responsible for some of the mixed effects observed in this study. As stated earlier in the limitations, the intervention used in this research (the formal CPG-use process) may not have been a valid measure of how completely CPG recommendations were incorporated into MTF standards of care. In other words, selection of subjects into groups may not have accurately reflected the level of exposure in either group to the recommendations of asthma CPGs. One indicator of how well asthma CPG recommendations have been adhered to is the rate at which asthmatics, even in the early stages of the disease, have been prescribed medications to specifically control the inflammation component of the

disease. Greater utilization of long-term controller (LTC) medications was one of the specific changes made between the recommendations of the first guidelines (1991) and those published in 1997.(3) It would be expected that if the asthma CPG guidelines were being followed as recommended, that the proportion of subjects prescribed LTCs would increase over time.

The results for the seventh hypothesis of this research found that the proportion of subjects treated with long-term control medications did not differ before and after the institution of asthma guidelines. The findings suggest that for all subjects, the proportion prescribed LTC medications increased significantly over the course of the study. For those exposed to the CPG-use process the proportion of subjects prescribed at least one LTC increased from 0.30 to 0.66 ($p < 0.001$), and for those not exposed to the formal CPG-use process the proportion of subjects prescribed at least one LTC increased from 0.30 to 0.65 ($p < 0.001$). The significant increase in the proportion of subjects prescribed a LTC is highly suggestive that providers in both groups were following CPG recommendations for treating asthma. If this is true, then it is also likely that the voluntary, and in some cases informal methods used by the Navy and Air Force to institutionalize asthma CPGs, were effective in creating the desired standardization of asthma care. This would support the notion that the formal CPG-use process, as an appropriate intervention for evaluating asthma outcomes, was not valid. That asthma CPG recommendations were being followed similarly across the services would also

explain why there was no observed difference between the groups, in at least some of the clinical outcomes evaluated.

Confounding was another possible explanation for the mixed results observed in this study. As discussed in Chapter Two, confounding can be thought of as a mixing of the effect of the exposure under study (CPG-use process) on the outcome with that of one or more factors. According to Hennekens, confounding can lead to an overestimate or underestimate of the true association between exposure and outcome and can even change the direction of the observed effect.⁽¹²³⁾ Assuming that the CPG recommendations were followed similarly between services, as suggested by the pattern of LTC prescribing, then one of the potential confounding variables could be the service type of the MTF in which treatment was received. To fully investigate this possibility is a matter for future research, however a brief comparison of results based on service type was possible with this data set. As mentioned previously, this involved replacing the CPG variable of the OLS model for each outcome with a categorical variable to represent service type. Although cost savings were no longer significant for the Army when analyzed this way, differences were observed in four of the five clinical outcomes between the Navy and Air Force. Compared to the Army, subjects treated at Air Force facilities experienced a significant decrease in beddays, exacerbations, and visits and a significant increase in prescriptions dispensed. For the Navy, only a significant increase in number of exacerbations, as compared to the Army, were observed.

As a further evaluation of inter-service differences in the approach to health care delivery, the mean change in outcomes was compared between the Navy and Air Force. Significant differences between the Air Force and Navy were reported for three outcomes (encounters, visits, and exacerbations), while in the remaining three other outcomes (cost, prescriptions dispensed, and beddays), the change was not significant.

This comparison does not provide conclusive evidence regarding basic differences between the services, however it is suggestive that asthma outcomes do vary by service type. A Medline search was conducted to determine if there was other published research that had investigated differences between military service types that would explain disease outcome difference. Although this search was unsuccessful in identifying specific research in this area, several studies were identified that discussed medical care differences between the branches of service. Mitchell, in describing the history of guideline use in the DoD alludes to significant diversity among the military branches in regards to their approach to both guidelines and disease management.(158) Wells and Murray also give this impression when describing the challenges that were faced by the leadership of previously autonomous MTFs when asked to restructure their health care delivery based upon centrally directed TRICARE health service regions (HSRs) with a Lead Agent. They state: "Strategic planning usually involves people who know each other and work together. Because of the joint nature of this effort, the members were unfamiliar with one another and with the other's systems".(13) Again, while not providing evidence that basic differences exist between the services in the way medical

care is delivered, these statements may be helpful in the establishment of a requirement for further research in this area.

Apart from the explanations mentioned above, the effect of the CPG-use process on asthma outcomes evaluated in this research may have varied depending whether care was received as an inpatient or outpatient. To evaluate this possibility, the inpatient and outpatient groups were analyzed independent of each other. After adjusting for covariates, the CPG-use process was associated with a significant reduction in cost in the inpatient group (\$1600, $p = 0.038$) but not in the outpatient group (\$9.57, $p = 0.093$). This would suggest that the cost savings associated with the CPG-use process, as observed in this research, were driven to a large extent by factors occurring in the inpatient setting. Two factors with the potential to influence the cost of providing inpatient therapy are the number of visits and the average length of stay for each visit. To test whether the CPG-use process had an effect on either of these factors, inpatient visits and inpatient beddays were compared between subjects exposed, and not exposed to the CPG-use process. As discussed earlier, although beddays did decrease significantly between the before and after period ($p = 0.001$ for both groups), there was no significant difference ($p = 0.08$) between the groups in the amount that beddays decreased during this period. Likewise, although the mean number of inpatient visits decreased from 0.706 to 0.156 ($p < 0.001$) and from 0.707 to 0.218 ($p < 0.001$) respectively for subjects exposed and not exposed to the CPG-use process, the number of inpatient visits did not

differ significantly between the groups in either the before ($p = 0.345$) or after ($p = 0.106$) periods.

Furthermore, although the risk of experiencing an acute care ($OR = 1.30$; 95%CI 1.25, to 1.34) or inpatient visit ($OR = 6.55$; 95%CI 4.94 to 8.68) was greater in the before period than after period, little of this risk reduction could be attributed to the CPG-use process. For those exposed to the CPG-use process there was a small, but significantly higher risk of experiencing an acute care visit ($OR = 1.15$; 95% CI: 1.11 to 1.19) as compared to subjects with no CPG-use exposure. There was no change in the risk of experiencing an asthma related hospitalization between those exposed, and not exposed, to the CPG-use process ($OR = 0.998$; 95% CI: 0.77 to 1.28). It would seem, therefore, that the decreased cost associated with the inpatient CPG-use group was not a function of fewer inpatient or acute care visits, but rather was due to some other factor or factors. Although not addressed in this research, differences in the delivery of health care between the services, such as the mix of licensed to non-licensed personnel involved in health care services, may be relevant and warrant further research.

5.3 Secondary Findings

In addition to service type, a number of other factors may have also acted as confounders in this research. Some of these factors were evaluated and reported as secondary findings. They included asthma severity, TRICARE region, beneficiary status of subject,

MTF size, age of subject, gender, presence of a respiratory comorbidity, treatment received at more than one facility, and treatment received at a lead agent facility

As mentioned briefly in the discussion regarding the effect of CPG-use on cost of asthma therapy, severity was evaluated using three OLS regression models. One model was based on a severity index consisting of three or more visits in the before period, another was based on the presence of one or more exacerbations in the before period, and the third was based on the extent of β -agonist inhaler use in the before period. The coefficients and p-values for these models are presented in Appendix F.

In none of the evaluations did severity significantly change the association between the CPG-use process and the outcomes of interest. Asthma severity was associated with significantly higher costs (\$444.40, $p < 0.001$) when evaluated by the presence of exacerbations, whereas when evaluated by the extent of β -agonist use (\$25.31, $p = 0.26$), or increased visits (\$6.90, $p = 0.774$) no significant increase was observed. In all models, subjects classified with a higher asthma severity in the before period were associated with a decrease in the number of encounters, visits, and prescriptions dispensed in the after period. The coefficients and p-values for these models are presented in Appendix F. Because of the acute nature of asthma exacerbations, these results are not totally unexpected. A flair-up of asthma in one period may be associated with numerous health care visits and prescriptions, however, once controlled, no other treatment might be sought until another exacerbation occurs, which in some cases can be very infrequently.

The effect of treatment within a specific TRICARE region on asthma outcomes is presented in Table C-1 of Appendix C. These results are consistent with reports in the literature that suggest that asthma outcomes vary considerably with geographic region.(41, 42) Overall, when compared to TRICARE region 1 (northeast), considerable cost variation occurred in six of the TRICARE regions. The most significant ($p < 0.001$) was a decrease of \$233 dollars per subject treated in region 11 (northwest) as compared to region 1. The number of asthma exacerbations that occurred also differed significantly by TRICARE region. Some variation also occurred between regions in the total number of health care encounters, visits, and prescriptions dispensed. The number of inpatient beddays was significantly different from the northeast region only in region 11 (northwest).

The results of this research were also suggestive of differences in asthma outcomes based upon beneficiary status, facility size, age, gender, treatment received in multiple facilities, the presence of a comorbid respiratory condition, and treatment received in a lead agent facility. These effects are presented in Appendix C, Tables C-2 through C-4.

As would be expected, because of the stringent recruitment and retainment standards regarding asthma, active duty personnel generally had better clinical outcomes than the other beneficiary groups. Both the number of health care encounters and prescriptions dispensed for active duty personnel were significantly lower than their dependents.

Although treatment costs were also lower than any of the other beneficiary categories, these results were not significant.

The size of the facility had a significant effect on some of the reported outcomes. Cost of therapy increased as facility size increased, but was only significantly different between the smallest facilities (< 250 observations) and the largest facilities (> 3000 observations), with costs at the larger facilities averaging just over \$250 more per subject over the nine-month period ($p < 0.001$). Clinical outcomes also were sensitive to facility size. Compared to facilities with 250 or less observations, total health care encounters increased significantly ($p < 0.01$ to $p < 0.001$) at all facilities, as did health care visits ($p < 0.001$ for all sizes). The number of prescriptions obtained were significantly different only in the mid-sized facilities of between 1001 to 2000 observations ($p = 0.035$). The risk of having an asthma exacerbation also was higher for those in larger facilities as compared to smaller facilities (OR = 3.59, $p < 0.001$). As discussed earlier, these results were not unexpected. The larger MTFs often act as referral centers because of their medical and personnel resources and therefore would be expected to treat the sicker patients.

Being treated at a lead agent facility had a similar effect on outcomes as did being treated in a larger facility. This is because since lead agent facilities are usually one of the largest MTFs in their TRICARE region, issues relevant to large facilities also apply to them.

Another factor that significantly affected asthma outcomes was age. For subjects between the 13 and 18 years of age, all outcomes evaluated, except for number of exacerbations, were significantly better than the referent group (5 to 12 yrs). Cost of therapy was \$92 ($p = 0.006$) less per subject. In addition, there were fewer encounters (0.74 per subject, $p < 0.001$), fewer visits (0.36 per subject, $p < 0.001$), fewer prescriptions (0.42 per subject, $p < 0.001$), and fewer beddays (0.169 per subject, $p < 0.001$) per subject. Although total visits and beddays were less for subjects 18 years of age and older, the risk of exacerbations was actually greater than the reference group ($OR = 1.27$, $p < 0.001$).

Males had significantly more encounters than females (0.21, $p < 0.001$), however this was primarily a function of an increased number of prescriptions as the total number of visits were lower for males compared to females (-0.051, $p < 0.001$). This research also found that males in general, had fewer days of hospitalization than females (-0.016, $p < 0.001$). As discussed in Chapter 2, reports in the literature are mixed regarding the effects of gender on asthma.(25, 44, 45, 51, 52)

Perhaps the most surprising of the secondary findings was the association between comorbid respiratory conditions as asthma outcomes. When both acute and chronic comorbidities were considered, the cost associated with treating asthma was non-significantly lower for those with comorbid conditions than those without comorbid

conditions. Similarly, with this definition of comorbidity, a number of the resource utilization measures also were lower for those with comorbid conditions. These included total number of encounters ($-0.49, p < 0.001$), prescriptions dispensed ($-0.56, p < 0.001$), and exacerbations ($OR = 0.71, 95\% CI: 0.64 \text{ to } 0.79$). However, when only chronic respiratory comorbidities were considered in the model, cost was significantly higher ($\$209.30, p = 0.003$) for those with the comorbid condition. There was also a significant increase in total visits ($0.46, p < 0.001$), and beddays ($0.049, p < 0.001$) when the chronic definition of comorbidity was applied to the models. The number of total encounters had non-significant increase ($0.1681, p = 0.241$) while prescriptions dispensed decreased non-significantly ($-0.09, p = 0.391$) for subjects with a chronic respiratory comorbidity. The number of exacerbations ($OR = 0.52; 95\% CI: 0.349 \text{ to } 0.767$) was lower even with this modified definition, than for subjects with no respiratory comorbidity. As previously noted, one explanation for these otherwise counterintuitive findings, especially when acute comorbidities were considered, was that both cost and resources could have been erroneously assigned to the competing diagnosis when a comorbidity was present.

As would be expected, the cost associated with subjects treated for asthma at multiple facilities was significantly higher ($\$206.85, p < 0.001$) than the cost for subjects treated at only one facility. The most likely explanation for the observed increase in cost was the corresponding increase in resources used as a result of using multiple facilities. Subjects utilizing more than one facility for asthma therapy had encounters encounters ($0.546, p < 0.002$), total visits ($0.494, p < 0.001$), prescriptions dispensed ($0.163, p < 0.001$), and

beddays (0.034, $p < 0.001$). There was, however, no significant change in the number of exacerbations experienced between those treated at multiple facilities and those treated at one facility.

5.4: Limitations

Several limitations should be kept in mind when interpreting the results of this research.

One of these was the definition of the asthma CPG use process. Although the Army Medical Department (AMEDD) has taken the lead in CPG promotion by providing a formal framework and timeframe for guideline implementation, dispersion of CPG standards throughout all three medical services has been substantial, both through formal and informal processes. The formal process used by the Army for implementing CPGs has been available to any DoD MTF upon request, as have the DoD asthma guidelines. Additionally, the NAEPP asthma guidelines, from which the DoD guidelines were patterned, have become recognized throughout the medical community as the standard of care for treating asthma – with or without the use of a formal implementation process. An example of an Air Force MTF that has successfully institutionalized asthma CPG standards of care is David Grant Medical Center at Travis AFB in California. In this case, the successful implementation of asthma CPGs was achieved in the context of a local, comprehensive, disease management program.⁽¹⁵⁸⁾ In a January 2002, the Population Health Support Division of the Air Force Medical Operations Agency (AFMOA/SGZZ), estimated that as of September of 2001, asthma CPG programs were in place at close to 60 percent of Air Force MTFs.⁽²¹¹⁾

For these reasons, the assumption that standardization of asthma care within the military health system was mainly a function of a formal CPG-use process may not be entirely valid. Both the formal and informal methods used by the Air Force and Navy to standardize asthma care within their services would bias the overall effect of CPG towards the null hypothesis.

Another limitation of this research was the assumption that the population of before/after asthma subjects included in this research was representative of all subjects treated for asthma within the military health system. This assumption was probably not valid for all subjects. As noted in the Chapter Four, the mean subject age was significantly different between the two groups with those in the matched group being slightly more than two years younger than those in the one period only group ($p < 0.0001$). There was also a difference in the groups based on gender. There were significantly more females in the before/after group than in the one period group ($p < 0.001$). There could also be a difference in severity between the before/after and one period groups. Although only a limited measure of severity was included in this research, it would make sense intuitively that those with repeated health care visits would have a more severe disease status (on average) than those with only single visits. Since the criteria for inclusion as a before/after subject was at least one repeat visit, as compared to a minimum of no repeat visits in the one period group, a severity issue might be a concern.

In addition to the difficulties involved with generalizing these results beyond the matched asthma pairs within the MHS population, there are also difficulties involved with trying to generalize these results outside of the DoD population. As discussed in Chapter Two, there are a number of factors that may make the military asthmatic population different from the general population. These include recruitment and retainment standards regarding a diagnosis of asthma and exposure to environmental and occupational risk factors.(6)

Another limitation of this research was the assumption that the majority of the asthma care for which the MHS was responsible, was captured by the databases used in this research. This assumption was most likely valid as long as the subject's primary or referral care was provided by a military MTF. However, once care was referred to a provider or treatment facility outside of the MTF network, the information became unavailable for analysis. As discussed in Chapter Three, the most likely time for this to occur would have been in the case of an asthma exacerbation or with the occurrence of a more severe case of asthma.

Another potential limitation of this study was the time-line. Because the institutionalization phase of the CPG intervention takes a considerable amount of time to take effect, a period of at least six months would have been more appropriate for the wash-out period. This was not possible however, since data were not available after September of 2001 for the purposes of this study.

Another limitation to this research was the heteroscedasticity of the data.

Heteroscedasticity can be caused by nonnormality of one of the variables or an indirect relationship between two or more of the variables. According to Wulder, heteroscedasticity is not fatal to an analysis, however the analysis is weakened and therefore care should be used in the interpretation of the results.(212)

5.5: Conclusions

Ho: 1: There is no difference in the direct costs associated with asthma therapy between individuals treated before, and individuals treated after the implementation of guidelines.

This hypothesis was rejected. Based on the results of this research, asthma therapy administered according to a formal guideline use process was associated with significantly lower costs than asthma therapy not based upon a formal guideline use process. This was true even after controlling for age, gender, and presence of respiratory comorbidity, facility size, and treatment received at multiple facilities or a lead agent facility, and beneficiary status. In this research, the formal CPG-use process was equivalent to treatment at an Army MTF. Therapy in the control group (no CPG-use) was equivalent to treatment at a Navy or Air Force facility. Therefore, another interpretation of the results of this research is that the cost of treating asthma in the Army is significantly less than the control group of Navy and Air Force.

Ho: 2: There is no difference, before and after the implementation of asthma guidelines, in the number of asthma related health care encounters for patients with a diagnosis of asthma.

After controlling for the effects of other factors, this hypothesis was not rejected. There was a significant reduction in the number of health care encounters experienced by subjects between the before and after periods, however this effect could not be attributed to exposure to the formal CPG-use process. Likewise, it cannot be said that subjects treated at Army MTFs experience few health care encounters than subjects treated at Navy or Air Force facilities.

Ho: 3: There is no difference, before and after the implementation of asthma guidelines, in the number of asthma related health care visits for patients with a diagnosis of asthma.

This hypothesis was rejected. As with total health care encounters there was a significant reduction in health care visits experienced by subjects between the before and after periods based upon the historical control group. In addition, after controlling for other factors there was a significant increase in number of health care visits for subjects exposed to the formal CPG-use process as compared to those in the control group. This association was opposite of what was expected. These results would also suggest that subjects treated for asthma at Army MTFs have significantly more health care visits than those treated at Navy or Air Force MTFs.

Ho: 4: There is no difference in the risk of experiencing an asthma exacerbation between individuals treated before guideline implementation and those treated after guideline implementation.

This hypothesis was rejected. As with total health care encounters and visits, there was a significant reduction in health care visits experienced by subjects between the before and after periods based upon the historical control group. After controlling for other factors there was a significant increase in number of exacerbations for subjects exposed to the formal CPG-use process as compared to those in the control group. This association was opposite of what was expected.

Ho: 5: There is no difference, before and after the implementation of asthma guidelines, in the number of prescriptions dispensed for asthma treatment.

After controlling for the effects of other factors, this hypothesis was not rejected. As with the other outcomes discussed above, there was a significant reduction in the number of prescriptions dispensed to subjects between the before and after periods, however this effect could not be attributed to exposure to the formal CPG-use process. Likewise, it cannot be said that subjects treated at Army MTFs are dispensed fewer prescriptions than subjects treated at Navy or Air Force facilities.

Ho: 6: There is no difference in length of hospital stay (for a primary diagnosis of asthma) between individuals treated at MTFs before asthma guidelines were instituted, and individuals treated at MTFs after asthma guidelines were instituted.

This hypothesis was not rejected. As with the other outcomes discussed above, there was a significant reduction in the average number of inpatient beddays per subject between the before and after periods, however this effect could not be attributed to exposure to the formal CPG-use process. Likewise, it cannot be said that subjects treated at Army MTFs experience fewer asthma related beddays than subjects treated at Navy or Air Force facilities.

Ho: 7: The proportion of asthma patients treated with long-term control medications does not differ before and after the institution of asthma guidelines.

This hypothesis was not rejected. A significantly higher proportion of subjects exposed to the formal CPG-use process as well as those in the control group were prescribed long-term controller medications in the after period as compared to the before period.

Although the change in LTC use was significantly greater in the CPG-use group than in the control, the proportional change (1%) between groups was not deemed to be clinically significant. Therefore, these results suggested that providers in both the CPG-use group and the control group had treated subjects according to CPG recommendations.

5.6: Implications for Decision Makers

Over the period of this research, the economic and clinical outcomes associated with asthma therapy improved significantly for both the CPG-use group and the control group. Based upon the consistency between the asthma CPG recommendation for an increased use of LTCs, and the actual increase in the proportion of LTCs prescribed during this time period, the observed outcome improvements do appear to be associated with better adherence to asthma CPG recommendations.

Although cost savings may vary based on the branch of service, the results of this research would suggest that the use of CPG recommendations do result in decreased cost. For this reason the medical departments of all three services should continue to promote standardization of asthma care as recommended by the DoD asthma CPGs. The use of a formal process to disseminate and institutionalize asthma CPG recommendations, as was done by the Army, appeared to result in better economic outcomes than the voluntary in informal methods used by the Navy and Air Force. Additional cost savings might be achieved by these services by adopting the formal CPG-use process of the Army.

The clinical outcomes evaluated in this research also improved over the course of this study. As with the improvement in the economic outcome, these improvements also appear to be associated with the asthma CPG recommendations. The use of a formal process, such as that by the Army to implement CPGs, does not appear to be associated

with any better clinical outcomes than the use of a voluntary an informal process for implementation.

Another advantage of standardizing care through the use of guidelines is that it facilitates quality improvement through feedback and comparison. As discussed by Kotter and Langelly, the use of similar outcome metrics within and between organizations allows for the establishment of common standards and baselines and thereby valid comparisons of outcomes.(114, 115) This makes it easier to translate successes experienced with outcomes at one site or facility to similar improvements in outcomes at other sites.

5.7: Recommendations for Further Research

There are several research projects that should be undertaken to expand and confirm the findings of this research. A survey could be used to better define which MTFs used guidelines in the treatment of asthma in this time period, and to determine the extent to which the guidelines were used. This would create a more accurate measure of the intervention that would permit a more valid comparison between services. Although developing and administering a survey would be time-intensive, the addition of the forthcoming information would be of great value in expanding the results of this research.

Other approaches to analysis may be useful as well. For instance, considering the MTF as the unit of analysis rather than the subject could be beneficial to MTF commanders who are interested in knowing how well asthma outcomes at their facilities compare to

outcomes at other facilities. Likewise, using a mixed model technique for analysis could be beneficial in that it would allow for all subjects to be evaluated, not just the matched pair. This would also improve the ability to generalize the results.

In addition, research conducted to evaluate differences in the way the way medical care is delivered between service branches may be useful. The results of this research project suggest that although the clinical outcomes of asthma are similar among the three branches of services, cost outcomes are not. Significant cost saving may be possible across the medical services of the Department of Defense through better understanding, and sharing, of each other's disease management systems.

APPENDIX A:
MEDICATIONS AND DOSAGES
FOR TREATING ASTHMA

Appendix A – Medications and Dosages for Treating Asthma

Medication	Dosage Form	Adult Dose	Child Dose	Indications
Long-Term-Control Medications				
Systemic Corticosteroids				
Methylprednisolone	2, 4, 8, 16, 32 mg tablets	<ul style="list-style-type: none"> 7.5-60 mg daily in a single dose or qod as needed for control 	<ul style="list-style-type: none"> 0.25-2mg/kg daily in single dose or qod as needed for control 	<ul style="list-style-type: none"> Long-term prevention of symptoms; suppression, control, and reversal of inflammation.
Prednisolone	5 mg tablets, 5mg/5cc, 5mg/5cc	<ul style="list-style-type: none"> Short-course "burst": 40-60 mg per day as single or 2 divided doses for 3-10 days 	<ul style="list-style-type: none"> Short course "burst": 1-2 mg/kg/day, maximum 60 mg/day, for 3-10 days 	<ul style="list-style-type: none"> For short term "burst": to gain prompt control of inadequately controlled persistent asthma.
Prednisone	1, 2.5, 5, 10, 20 2.5 mg tablets; 5 mg/cc, 5mg/5cc	<ul style="list-style-type: none"> Short-course "burst": 40-60 mg per day as single or 2 divided doses for 3-10 days 	<ul style="list-style-type: none"> Short course "burst": 1-2 mg/kg/day, maximum 60 mg/day, for 3-10 days 	
Cromolyn and Nedocromil				
Cromolyn	Meter dose inhaler (MDI) 1 mg/puff Nebulizer Sol'n 20 mg/ampule	<ul style="list-style-type: none"> 2-4 puffs tid-qid 1 ampule tid-qid 	<ul style="list-style-type: none"> 2 puffs tid-qid 1 ampule tid-qid 	<ul style="list-style-type: none"> Long-term prevention of symptoms; may modify inflammation.
Nedocromil	MDI 1.75 mg/puff	<ul style="list-style-type: none"> 2-4 puffs bid-qid 	<ul style="list-style-type: none"> 1-2 puffs bid-qid 	<ul style="list-style-type: none"> Preventive treatment prior to exercise or known allergen.
Long-Acting β_2-Agonists				
Salmeterol	Inhaled MDI 21 mcg/puff, 60 or 120 puffs DPI50 mcg/blister	<ul style="list-style-type: none"> 2 puffs 1 12 hours 1 blister q 12 hours 	<ul style="list-style-type: none"> 1-2 puffs q 12 hours 1 blister q 12 hours 	<ul style="list-style-type: none"> Long-term prevention of symptoms, especially nocturnal symptoms, added to anti-inflammatory therapy
Sustained-Release Albuterol	tablet 4 mg tablet	<ul style="list-style-type: none"> 4mg q 12 hours 	<ul style="list-style-type: none"> 0.3-0.6 mg/kg/day, not to exceed 8 mg/day 	<ul style="list-style-type: none"> Prevention of exercise-induced bronchospasm

Appendix A – Medications and Dosages for Treating Asthma

Medication	Dosage Form	Adult Dose	Child Dose	Indications
Long-Term-Control Medications				
Systemic Corticosteroids				
Methylprednisolone	2, 4, 8, 16, 32 mg tablets	● 7.5-60 mg daily in a single dose or qod as needed for control	● 0.25-2mg/kg daily in single dose or qod as needed for control.	● Long-term prevention of symptoms; suppression, control, and reversal of inflammation.
Prednisolone	5 mg tablets, 5mg/5cc, 5mg/5cc	● Short-course "burst": 40-60 mg per day as single or 2 divided doses for 3-10 days	● Short course "burst": 1-2 mg/kg/day, maximum 60 mg/day, for 3-10 days	● For short term "burst": to gain prompt control of inadequately controlled persistent asthma.
Prednisone	1, 2.5, 5, 10, 20, 25 mg tablets; 5 mg/cc, 5mg/5cc	● Short-course "burst": 40-60 mg per day as single or 2 divided doses for 3-10 days	● Short course "burst": 1-2 mg/kg/day, maximum 60 mg/day, for 3-10 days	
Cromolyn and Nedocromil				
Cromolyn	Meter dose inhaler (MDI) 1 mg/puff Nebulizer Sol'n 20 mg/ampule	● 2-4 puffs tid-qid ● 1 ampule tid-qid	● 2 puffs tid-qid ● 1 ampule tid-qid	● Long-term prevention of symptoms; may modify inflammation.
Nedocromil	MDI 1.75 mg/puff	● 2-4 puffs bid-qid	● 1-2 puffs bid-qid	● Preventive treatment prior to exercise or known allergen.
Long-Acting β_2-Agonists				
Salmeterol	Inhaled MDI 21 mcg/puff, 60 or 120 puffs DPI 50 mcg/blister	● 2 puffs 1 12 hours ● 1 blister q 12 hours	● 1-2 puffs q 12 hours ● 1 blister q 12 hours	● Long-term prevention of symptoms, especially nocturnal symptoms,, added to anti-inflammatory therapy
Sustained-Release Albuterol	tablet 4 mg tablet	● 4mg q 12 hours	● 0.3-0.6 mg/kg/day, not to exceed 8 mg/day	● Prevention of exercise-induced bronchospasm

Medication	Dosage Form	Adult Dose	Child Dose	Indications
Quick-Relief Medications				
<i>Short-Acting Inhaled Beta₂-Agonists</i>				
	(MDI)			
Albuterol	90 mcg/puff	● 2 puffs 5 min prior to exercise	● 1-2 puffs 5 minutes prior to exercise	● Relief of acute symptoms; quick relief medication
Albuterol HFA	90 mcg/puff	● 2 puffs tid-qid prn	● 2 puffs tid-qid prn	
Bitolterol	370 mcg/puff			
Pirbuterol	200 mcg/puff			
Terbutaline	200 mcg/puff			● Preventive treatment Prior to exercise for exercise-induced bronchospasm.
Albuterol Rotahaler	<u>Dry Powder Inhaler (DPI)</u> 200 mcg/capsule	● 1-2 capsules q 4-6 hours as needed and prior to exercise.	● 1 capsule q 4-6 hours as needed and prior to exercise.	
Albuterol	<u>Nebulizer Solution</u> 5 mg/ml (0.5%)	● 1.25-5 mg (.25-1 cc) in 2-3 cc of saline q 4-8 hours	● 0.05 mg/kg (min 1.25 mg, max 2.5mg) in 2-3 cc of saline q 4-6 hours	
Bitolterol	2 mg/ml (0.2%)	● 0.5-3.5 mg (.25-1cc) in 2-3 cc of saline q 4-8 hours	● Not established	
Anticholinergics				
Ipratropium	MDI 18 mcg/puff Nebulizer Solution .25 mg/ml (0.025%)	● 2-3 puffs q 6 hours ● 0.25 mg q 6 hours	● 1-2 puffs q 6 hours ● 0.25-0.5 mg q 6 hours	● Relief of acute bronchospasm

Appendix A – Medications and Dosages for Treating Asthma (Continued)

Medication	Dosage Form	Adult Dose	Child Dose	Indications
Quick-Relief Medications				
<i>Systemic Corticosteroids</i> Methylprednisolone	2, 4, 8, 16, 32 mg tablets	<ul style="list-style-type: none"> Short course "burst": 40-60 mg/day as single or 2 divided doses for 3-10 days 	<i>(Applies to all three systemic corticosteroids)</i> <ul style="list-style-type: none"> Short course "burst": 1-2mg/kg/day, max of 60 mg/day, for 3-10 days 	For moderate-to-severe exacerbations to prevent progression of exacerbation, reverse inflammation, speed recovery, and reduce rate of relapse.
Prednisolone	5 mg tabs, 5 mg/5cc, 15 mg/5cc			
Prednisone	1, 2.5, 5, 10, 20, 25 mg tabs; 5 mg/cc 5 mg/5 cc			

APPENDIX B:

WORKSHEET FOR ADDRESSING INTERNAL VALIDITY
ISSUES IN A BEFORE-AFTER DESIGN

APPENDIX B:

Worksheet for Addressing Internal Validity Issues in a Before-After Design

This worksheet was developed for a before-after design used to examine the effects of instituting guidelines for asthma care on the outcomes of care. In this case the independent variable is the implementation of guidelines and the control group is the group that received care under the old system which did not use guidelines. Therefore the worksheet was developed for a single hypothesis and a specific disease state.

Possible dependent variables include: cost of care, number of repeat visits, number of hospitalizations, and length of stay either in the ED or the hospital.

The example worksheet shown below has been completed for a proposed study of guidelines used by the armed forces to treat members of the armed forces and their dependents. The source of the data will be a database; hence the study is retrospective, observational, and analytic. The comparison groups will be the 'before' group, patients treated within a year before guidelines were implemented, and the 'after' group, patients with asthma treated within a year after implementation.

<i>Internal Validity Issue</i>	<i>Methods Proposed to Address Issue</i>
Unit of analysis (e.g. using visits as the unit of analysis results in having the same patient appear multiple times within each group and in having the same patient appear in both the control and the guideline group)	This study will use the patient as the unit of analysis so that no patient will be included more than once within each group; data on additional visits will be included in the dependent variables, i.e. number of visits etc. However the same patient might appear in both the control and guideline groups. These patients will be identified and data reported on relevant variables to assess the possible impact on the study.
Temporal remoteness (e.g. the control group was treated in much earlier time period so that multiple aspects of the treatment of asthma likely have changed)	Study adjacent time periods and restrict the length of the time periods. In this study, each time period will be one year in length and the guideline group will be the year immediately following implementation of the guidelines. Specific issues related to differences in time period are addressed below.
Bias in recording data (e.g. data is recorded in greater detail after guidelines are implemented)	Guidelines could result in bias in data recording for the guideline group. Comparison of the proportion of patients dropped from each group for missing data should indicate if this problem is likely.
Bias in extracting data (e.g. charts are more carefully read for patients in the guideline group than for the control group)	The data source for this study is a database. All data will be extracted using data commands that will be the same for both groups so there should be no bias in data extraction.

APPENDIX B

Worksheet for Addressing Internal Validity Issues in a Before-After Design -*Continued*

<i>Internal Validity Issue</i>	<i>Methods Proposed to Address Issue</i>
Selection bias (e.g. patients with severe disease in the guideline group are more likely to be found not eligible for inclusion in the study)	Persons who determine the eligibility of a patient for the study should be blind to treatment group. In this study, eligibility will be determined using data commands which will be the same for both groups so selection bias does not seem likely.
Confounding caused by contamination of the control group (e.g. a majority of physicians are treating patients according to similar guidelines before the institutional guidelines are implemented)	Describe treatment provided on key variables; e.g. use of steroids during each data collection period.
Confounding resulting from the introduction of new treatment modalities (e.g. treatment under the old system did not include use of ...)	Describe treatments available under both old and new system to identify differences; review formularies relevant to each group to identify addition of new therapies.
Confounding resulting from seasonal variations or differences in environment (e.g. allergy season is unusually severe during one data collection period or environment changes when mining or agriculture is stopped or started)	Seasonal variations or environmental concerns should not be an issue in this study because multiple institutions from several areas of the country will be included.
Confounding resulting from changes in the population served (e.g. the institution served primarily insured patients during the control period and but also served Medicaid patients during the guideline period)	Describe samples on relevant variables; type of insurance, severity of illness, age, and gender. This should not be an issue in this study because all patients are from the military and the time frame is short enough (two years total) that global changes in the severity of asthma should be minimal.
Confounding resulting from other policy changes (e.g. criteria for hospital admission, length of stay, changes in accounting procedures, etc.)	Changes in policy other than the use of guidelines seems possible. Review of policies from a sample of the institutions included can clarify whether changes in policy are likely to be an issue.
Strength of the intervention. The guidelines could have little impact on actual practice so that no differences in outcomes are observed.	Describe treatment provided during each data collection period on key variables; e.g. use of steroids.

Adapted from: Slack MK, Bennett DM: Issues in Using a Before-After Study Design to Assess the Effect of Clinical Practice Guidelines: The Example of Asthma. 2001 - Unpublished

APPENDIX C: SUMMARY TABLES
OF EFFECT OF INDEPENDENT
VARIABLES ON OUTCOMES

TABLES C-1 THROUGH C-5

TABLE C-1: Results Of Regression Models For Effect Of Tricare Region On Outcomes

TRICARE Region	Statistics	Cost	Encounters	Visits	Prescrip- tions	Exacer- bations	Beddays
Region 1 Northeast (Referent)	Coef. (OR)	0.000	0.000	0.000	0.000	0.000	0.000
	Std. Error	N/A	N/A	N/A	N/A	N/A	N/A
	t or [z] statistic	N/A	N/A	N/A	N/A	N/A	N/A
	p-value	N/A	N/A	N/A	N/A	N/A	N/A
Region 2 Mid-Atlantic	Coef. (OR)	-60.913	0.335	0.219	0.099	(2.707)	-0.006
	Std. Error	46.061	0.093	0.045	0.068	0.323	0.008
	t or [z] statistic	1.32	3.61	4.88	1.45	[8.33]	-0.75
	p-value	0.186	<0.001	<0.001	0.147	<0.001	0.454
Region 3 Southeast	Coef. (OR)	-127.606	-0.185	-0.211	0.053	(1.570)	-0.003
	Std. Error	48.357	0.098	0.047	0.071	0.215	0.009
	t or [z] statistic	-2.64	-1.89	-4.47	0.74	[3.30]	-0.35
	p-value	0.008	0.059	<0.001	0.461	<0.001	0.726
Region 4 Gulfsouth	Coef. (OR)	-105.306	-0.078	0.110	-0.053	(1.446)	-0.007
	Std. Error	60.531	0.122	0.059	0.089	0.233	0.011
	t or [z] statistic	-1.74	-0.63	1.87	-0.59	[2.28]	-0.63
	p-value	0.082	0.526	0.062	0.556	0.022	0.531
Region 5 Heartland	Coef. (OR)	-92.571	-0.015	0.043	-0.089	(1.103)	-0.014
	Std. Error	58.427	0.118	0.057	0.086	0.177	0.011
	t or [z] statistic	-1.58	-0.13	0.76	-1.03	[0.61]	-1.32
	p-value	0.113	0.896	0.449	0.304	0.539	0.186
Region 6 Southwest	Coef. (OR)	-112.375	-0.127	-0.079	0.012	(1.450)	0.002
	Std. Error	45.069	0.091	0.044	0.067	0.185	0.008
	t or [z] statistic	-2.49	-1.40	-1.79	0.17	[2.91]	0.28
	p-value	0.013	0.162	0.073	0.862	0.004	0.776
Region 7/8 Central	Coef. (OR)	-88.378	0.069	-0.107	0.211	(1.655)	-0.004
	Std. Error	44.614	0.090	0.044	0.066	0.207	0.008
	t or [z] statistic	-1.98	0.76	-2.45	3.200	[4.03]	-0.084
	p-value	0.048	0.446	0.014	<0.001	<0.001	0.614
Region 9 Southern California	Coef. (OR)	-113.484	-0.031	0.226	-0.233	(1.513)	-0.009
	Std. Error	52.371	0.106	0.051	0.077	0.220	0.009
	t or [z] statistic	-2170	-0.29	4.430	-3.01	[2.85]	-0.93
	p-value	0.030	0.771	<0.001	0.003	0.004	0.354

TABLE C-1: Results Of Regression Models For Effect Of Tricare Region On Asthma Outcomes - *continued*

TRICARE Region	Statistics	Cost	Encounters	Visits	Prescrip- tions	Exacer- bations	Beddays
Region 10 Golden Gate	Coef. (OR)	-169.924	0.016	0.060	0.044	(0.235)	-0.027
	Std. Error	84.310	0.171	0.082	0.125	0.093	0.015
	t or [z] statistic	-2.02	0.10	0.73	0.36	[-3.65]	-1.73
	p-value	0.044	0.924	0.463	0.722	<0.001	0.084
Region 11 Northwest	Coef. (OR)	-233.280	-0.398	-0.230	-0.173	(1.154)	-0.035
	Std. Error	63.529	0.129	0.062	0.094	0.189	0.012
	t or [z] statistic	-3.67	-3.10	-3.70	-1.84	[0.880]	-3.03
	p-value	<0.001	0.002	<0.001	0.065	.380	0.002
Region 12 Non- continental	Coef. (OR)	-1.604	0.233	0.245	0.006	(2.262)	0.015
	Std. Error	43.823	0.089	0.043	0.065	0.283	0.008
	t or [z] statistic	-0.04	2.63	5.740	0.090	[6.51]	1.95
	p-value	0.971	0.009	<0.001	0.928	<0.001	0.052

TABLE C-2: Results Of Regression Models For Effect Of Beneficiary Status On Asthma Outcomes

<i>Beneficiary Status of Subject</i>	<i>Statistics</i>	<i>Cost</i>	<i>Encounters</i>	<i>Visits</i>	<i>Prescriptions</i>	<i>Exacerbations</i>	<i>Beddays</i>
Dependent of active duty member (Referent Category)	Coef. (OR)	0.000	0.000	0.000	0.000	N/A	N/A
	Std. Error	N/A	N/A	N/A	N/A	N/A	N/A
	t or [z] statistic	N/A	N/A	N/A	N/A	N/A	N/A
	p-value	N/A	N/A	N/A	N/A	N/A	N/A
Retired	Coef. (OR)	165.645	0.330	-0.175	0.412	N/A	N/A
	Std. Error	130.623	0.264	0.127	0.193	N/A	N/A
	t or [z] statistic	1.270	1.250	-1.380	2.130	N/A	N/A
	p-value	0.205	0.211	0.169	0.033	N/A	N/A
Dependent of retired	Coef. (OR)	43.168	0.150	-0.005	0.085	N/A	N/A
	Std. Error	33.933	0.069	0.033	0.050	N/A	N/A
	t or [z] statistic	1.270	2.180	-0.170	1.700	N/A	N/A
	p-value	0.203	0.029	0.869	0.089	N/A	N/A
Active duty member	Coef. (OR)	-11.871	-0.484	0.041	-0.373	N/A	N/A
	Std. Error	38.140	0.077	0.037	0.056	N/A	N/A
	t or [z] statistic	-0.310	-6.270	1.090	-6.620	N/A	N/A
	p-value	0.756	<0.001	0.274	<0.001	N/A	N/A
Active duty and dependents vs retirees and dependents	Coef. (OR)	N/A	N/A	N/A	N/A	(0.806)	-0.008
	Std. Error	N/A	N/A	N/A	N/A	0.059	0.006
	t or [z] statistic	N/A	N/A	N/A	N/A	[-2.950]	-1.280
	p-value	N/A	N/A	N/A	N/A	0.003	0.202

TABLE C-3: Results Of Regression Models For Effect Of Facility Size On Asthma Outcomes

<i>MTF Size based on observations</i>	<i>Statistics</i>	<i>Cost</i>	<i>Encounters</i>	<i>Visits</i>	<i>Prescriptions</i>	<i>Exacerbations</i>	<i>Beddays</i>
0 to 250 observations (Referent Category)	Coef. (OR)	0.000	0.000	0.000	0.000	0.000	0.000
	Std. Error	N/A	N/A	N/A	N/A	N/A	N/A
	t or [z] statistic	N/A	N/A	N/A	N/A	N/A	N/A
	p-value	N/A	N/A	N/A	N/A	N/A	N/A
251 to 500 observations	Coef. (OR)	77.731	0.284	0.157	0.140	N/A	N/A
	Std. Error	90.989	0.184	0.089	0.134	N/A	N/A
	t or [z] statistic	0.850	1.540	1.770	1.050	N/A	N/A
	p-value	0.393	0.123	0.077	0.294	N/A	N/A
501 to 1000 observations	Coef. (OR)	78.478	0.428	0.292	0.178	N/A	N/A
	Std. Error	83.617	0.169	0.081	0.123	N/A	N/A
	t or [z] statistic	0.940	2.530	3.590	1.440	N/A	N/A
	p-value	0.348	0.011	<0.001	0.150	N/A	N/A
1001 to 2000 observations	Coef. (OR)	103.815	0.553	0.373	0.232	N/A	N/A
	Std. Error	74.634	0.151	0.073	0.110	N/A	N/A
	t or [z] statistic	1.390	3.660	5.120	2.100	N/A	N/A
	p-value	0.164	<0.001	<0.001	0.035	N/A	N/A
2001 to 3000 observations	Coef. (OR)	115.927	0.588	0.527	0.110	N/A	N/A
	Std. Error	76.053	0.154	0.074	0.112	N/A	N/A
	t or [z] statistic	1.520	3.820	7.100	0.980	N/A	N/A
	p-value	0.127	<0.001	<0.001	0.326	N/A	N/A
More than 3000 observations	Coef. (OR)	262.910	0.657	0.696	0.095	N/A	N/A
	Std. Error	71.976	0.146	0.070	0.106	N/A	N/A
	t or [z] statistic	3.650	4.150	9.900	0.890	N/A	N/A
	p-value	<0.001	<0.001	<0.001	0.372	N/A	N/A
More than 2000 as compared to less than 2000 observations	Coef. (OR)	N/A	N/A	N/A	N/A	(3.590)	0.012
	Std. Error	N/A	N/A	N/A	N/A	0.336	0.002
	t or [z] statistic	N/A	N/A	N/A	N/A	[13.650]	7.020
	p-value	N/A	N/A	N/A	N/A	<0.001	<0.001

TABLE C-4: Results Of Regression Models For Effect Of Age On Asthma Outcomes

<i>Age Category of Subject</i>	<i>Statistics</i>	<i>Cost</i>	<i>Encounters</i>	<i>Visits</i>	<i>Prescriptions</i>	<i>Exacerbations</i>	<i>Beddays</i>
Five to twelve years of age (Referent Category)	Coef. (OR)	0.000	0.000	0.000	0.000	N/A	N/A
	Std. Error	N/A	N/A	N/A	N/A	N/A	N/A
	t or [z] statistic	N/A	N/A	N/A	N/A	N/A	N/A
	p-value	N/A	N/A	N/A	N/A	N/A	N/A
Thirteen to eighteen years of age	Coef. (OR)	-92.020	-0.742	-0.359	-0.4253	(-0.94)	0.16126
	Std. Error	33.459	0.068	0.033	0.0494	0.078	0.0439
	t or [z] statistic	-2.750	-10.970	-11.000	-8.600	[-0.74]	3.670
	p-value	0.006	<0.001	<0.001	<0.001	0.457	<0.001
Nineteen to forty years of age	Coef. (OR)	12.840	0.118	-0.181	0.223	(1.27)	0.1511
	Std. Error	30.291	0.061	0.030	0.045	0.075	0.03128
	t or [z] statistic	0.420	1.920	-6.120	4.980	[4.090]	4.830
	p-value	0.672	0.055	<0.001	<0.001	<0.001	<0.001

TABLE C-5: Results Of Regression Models For Effect Of Gender, Comorbid Respiratory Conditions, Treatment In Multiple Facilities, And Treatment In A Lead Agent Facility On Asthma Outcomes

<i>Variable</i>	<i>Statistics</i>	<i>Cost</i>	<i>Encounters</i>	<i>Visits</i>	<i>Prescrip- tions</i>	<i>Exacer- bations</i>	<i>Beddays</i>
Males as compared to females	Coef. (OR)	-19.688	0.209	-0.051	0.177	(-1.04)	-0.016
	Std. Error	25.031	0.051	0.024	0.037	0.024	0.004
	<i>t</i> or [<i>z</i>] statistic	-0.790	4.120	-210.000	4.780	[-1.11]	-3.81
	<i>p-value</i>	0.764	<0.001	0.036	<0.001	0.268	<0.001
Comorbid vs no-Comorbid	Coef. (OR)	-6.670	-0.489	0.399	-0.562	(0.71)	-0.003
	Std. Error	22.178	0.045	0.022	0.033	0.037	0.004
	<i>t</i> or [<i>z</i>] statistic	-0.300	-10.840	18.430	-16.880	[-6.53]	-0.69
	<i>p-value</i>	0.764	<0.001	<0.001	<0.001	<0.001	0.492
Multiple facilities vs single facility	Coef. (OR)	206.855	0.546	0.494	0.163	(0.928)	0.034
	Std. Error	28.390	0.058	0.028	0.042	0.064	0.005
	<i>t</i> or [<i>z</i>] statistic	7.280	9.480	17.760	3.890	[-1.08]	6.71
	<i>p-value</i>	<0.001	<0.001	<0.001	<0.001	0.279	<0.001
Lead agent facility vs other MTF	Coef. (OR)	153.380	0.024	-0.009	0.001	(1.930)	0.070
	Std. Error	34.623	0.070	0.034	0.051	0.125	0.006
	<i>t</i> or [<i>z</i>] statistic	4.780	0.340	-0.270	0.020	[10.16]	11.22
	<i>p-value</i>	<0.001	0.732	0.787	0.986	<0.001	<0.001

APPENDIX D

LIST OF VARIABLES INCLUDED IN
DATABASE RECEIVED FROM
THE DoD PHARMACOECONOMIC CENTER

APPENDIX D: Inpatient And Outpatient Variable Tables

Variable	Description
ptID	Patient ID
ampulVisit	Ambulatory Proc Visit Flag
apg1	Ambulatory Patient Group 1 - Medical
adjRVU	Adjusted RVU, Raw
totAdjRVU	Aggregate APG Weight, Raw
totAggAPG	Aggregate APG, Total
EBCPrice	EBC Price, Raw
totEBCPrice	EBC Price, Total
full cost	Full Cost, Raw
totFulCost	Full Cost Total
smplRVU	Simple RVU, Raw
totSmplRVU	Simple RVU, Total
varCost	Variable Cost, Raw
totVarCost	Variable Cost, Total
visits	Visits, Raw
totVisits	Visits, Total
age	Age
apg2	Ambulatory Patient Group 2 E and M
apg3	Ambulatory Patient Group 3 - Proc
apg4	Ambulatory Patient Group 4 - Proc
apg5	Ambulatory Patient Group 5 - Proc
apg6	Ambulatory Patient Group 6 - Proc
cm	Calendar Month
cy	Calendar Year
comBenCat	Common Beneficiary Category
dob	Date of Birth
dx1	Diagnosis 1
dx2	Diagnosis 2
dx3	Diagnosis 3
dx4	Diagnosis 4
dispCd	Disposition Code
eandM	Evaluation and Management Code
fy	Fiscal Year
fm	Fiscal Month
fmp	Family Member Prefix
gender	Gender
inpatient	Inpatient Indicator
marital	Marital Status

APPENDIX D: Inpatient And Outpatient Variable Tables *-continued*

Variable	Description
meprs	MEPERS (3) Code
PCMtype	Primary Care Manager ID Type
proc1	CPT4 Procedure 1
proc2	CPT4 Procedure 2
proc3	CPT4 Procedure 3
proc4	CPT4 Procedure 4
provSpCy	Provider Specialty
svcDate	Service Date
sponPayGrd	Sponsor Pay Grade
sponSvc	Sponsor Service
tmtID	Treatment Center DMIS ID
tmtMilDep	Tmt DMIS Mil Dep
tmtName	Tmt DMIS Name
tmtParID	Tmt Parent DMIS id
tmtParName	Tmt Parent DMIS Name
tmtSvcClin	Tmt Service Clinic

Pharmacy Table

ptID	Patient Identification
generic	Standard Generic Name of Medication
NDC	National Drug Code Number
genInpt	Generic Name of Prescription
product	Medication Name
doseForm	Dosage Form (TAB, CAP, SURP, GEL, etc)
strength	Number of Units in Dosage Form
defUnit	Default Unit
AHFS	AHFS Code
RxNbr	Prescription Number
fillDate1	Date of This Fill (coded)
fillDtSas	SAS Date of This Fill
action	N for new Rx, R for Refill
qty	Quantity of This Fill
fillNbr	Fill Number
cost	Cost
ptCat	Category of the Patient
arStat	Active/Retired Status
pGrade	Pay Grade (Rank) of Sponsor

APPENDIX D: Inpatient And Outpatient Variable Tables - *continued*

Variable	Description
sex	Sex of Patient
age	Age of Patient
racPop	Race of Patient
provClass	Classification of Provider
parDMIS	Parent DMIS ID
fillDate2	Fill Date in YYYYMM Format
fmp	Family Member Prefix
filldate	Fill Date in YYYYMMDD Format
specMTF	Specific Military Treatment Facility
svc	Branch of Service
type	Origin of Script (CHAMPUS or Military)
dodReg	DoD Region

APPENDIX E

LETTERS OF APPROVAL FOR RECEIPT OF DATA FROM THE DOD
PHARMACOECONOMIC CENTER AND THE UNIVERSITY OF ARIZONA
HUMAN SUBJECTS PROGRAM

Department of Pharmacy Practice & Science

- Clinical Pharmacy Division
- Social and Administrative Sciences Division
- Pharmaceutical Sciences Division



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P.O. Box 210207
Tucson, Arizona 85721-0207
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10 October, 2001

CAPT Joseph C. Torkildson, MC, USN
DoD Pharmacoeconomic Center
2421 Dickman Road
Bldg 1001, Room 310
Fort Sam Houston, TX 78234-5081

Sir,

I am an active duty Major in the United States Air Force on official orders from the Air Force Institute of Technology (AFIT) to complete a Doctors of Philosophy degree in pharmacy practice at the University of Arizona in Tucson, AZ. I have completed the didactic and examination requirements of the program and am now working towards fulfilling the dissertation requirement. As part of the dissertation process, I am required to conduct original research and data analysis. The topic that I am pursuing involves the evaluation of guideline use on the economic and clinical outcomes of asthma within the Department of Defense environment.

I am writing to request permission to conduct data analysis on several sets of Department of Defense data available through your office. Specifically I am requesting data for the period between 1 January 1997 and 30 September 2001 from the Uniformed Services Prescription Database and the ARS-Bridge, which include variables from the Standard Inpatient Data Record and the Standard Ambulatory Data Record. The ICD-9 codes I am interested in include those between 493.0 – 493.9 (asthma). My research will not require any personal identifiers; once the data sets have been merged and a unique identifier created for each record, variables that could be problematic in terms of confidentiality issues, such as the SSN, can be removed.

Thank you for your consideration of this request for data. Once your office has determined that the above-mentioned data may be released, a proposal will be submitted to the University of Arizona Institutional Review Board (IRB) outlining the study. A copy of the action taken by the University of Arizona IRB will be submitted to you before the release of any data.

Sincerely,

A handwritten signature in cursive script, appearing to read "David M. Bennett".

David M. Bennett, Maj, USAF, BSC
Ph.D. Candidate, University of Arizona

DoD Pharmacoeconomic Center
2421 Dickman Road
Building 1001, Room 310
Fort Sam Houston, TX 78234-5081

23 October 2001

Maj David Bennett, USAF, BSC
Ph.D. Candidate, University of Arizona
C/O College of Pharmacy
University of Arizona
1703 Mabel Street
Tucson, AZ 85721-0207


Dear Maj Bennett:

I have reviewed your request for permission to analyze Department of Defense data either controlled by or available to this office as a required part of your doctoral program in pharmacy practice. Although the data from different sources will be collated using data fields subject to protection under the Privacy Act of 1974, the final data product requested will contain no such identifiers. Also, your participation in this program on orders from the AFIT, in my opinion, creates a situation in which you have a legitimate argument to have access to the data on the basis of an official "need to know". Therefore, I have no difficulty in approving your request for this data file.

I would remind you that permission to have access to and analyze the data does not constitute approval by the Department of Defense to publish the results of your analysis in the public domain. If at the conclusion of your project you wish to publish the results of your analysis, you will need to secure such approval from the appropriate channels.

I wish you luck in completing your project. As soon as we receive notification that the University of Arizona IRB has approved your project we will forward the requested data to you.

Sincerely,



CAPT Joseph C. Torkildson, MC, USN
Director of Clinical Operations
DoD Pharmacoeconomic Center

Human Subjects Protection Program

THE UNIVERSITY OF
ARIZONA.
TUCSON ARIZONA

1350 N. Vine Avenue
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Tucson, AZ 85724-5137
(520) 626-6721

28 November 2001

Daniel C. Malone, Ph.D.
David Bennett, Ph.D. Candidate
Department of Pharmacy Practice/Science
College of Pharmacy
PO BOX 210207

**RE: EFFECTIVENESS OF CLINICAL PRACTICE GUIDELINES FOR TREATING
ASTHMA IN THE DEPARTMENT OF DEFENSE: A COMPARISON OF CLINICAL
AND ECONOMIC OUTCOMES BETWEEN THE ARMY, AIR FORCE, AND NAVY**

Dear Dr. Malone and Mr. Bennett:

We received documents concerning your above cited project. This study involves analysis of existing data (to be provided by the Department of Defense Pharmacoeconomic Center without identifiers). Therefore, regulations published by the U.S. Department of Health and Human Services [45 CFR Part 46.101(b) (4)] exempt this type of research from review by our Institutional Review Board.

Thank you for informing us of your work. If you have any questions concerning the above, please contact this office.

Sincerely,



Rebecca Dahl, R.N., Ph.D.
Director
Human Subjects Protection Program

RD/js
cc: Departmental/College Review Committee

APPENDIX F:

THE EFFECT OF A SEVERITY COVARIATE ON PREDICTING ASTHMA
OUTCOMES USING OLS REGRESSION MODELS

Table F-S1: OLS regression model predicting total cost adjusting for severity (more than three visits in the before period)

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-55.662	24.076	-2.310	0.021	-102.850	-8.474
Cost - before	0.273	0.003	93.950	<0.001	0.267	0.278
Males	-19.590	25.033	-0.780	0.434	-68.655	29.476
Comorbidity	-6.990	22.206	-0.310	0.753	-50.514	36.534
Region 1	Referent Group					
Region 2	-60.711	46.066	-1.320	0.188	-151.001	29.579
Region 3	-127.603	48.358	-2.640	0.008	-222.383	-32.822
Region 4	-105.352	60.532	-1.740	0.082	-223.995	13.291
Region 5	-92.499	58.428	-1.580	0.113	-207.018	22.019
Region 6	-112.690	45.083	-2.500	0.012	-201.052	-24.328
Region 7/8	-88.507	44.616	-1.980	0.047	-175.955	-1.059
Region 9	-113.037	52.394	-2.160	0.031	-215.730	-10.345
Region 10	-169.910	84.310	-2.020	0.044	-335.158	-4.663
Region 11	-233.026	63.535	-3.670	<0.001	-357.555	-108.498
Non-conus	-1.720	43.825	-0.040	0.969	-87.617	84.178
Multiple facilities	205.875	28.599	7.200	<0.001	149.820	261.929
0 to 250	Referent Group					
251 to 500	77.749	90.990	0.850	0.393	-100.592	256.089
501 to 1000	78.215	83.623	0.940	0.350	-85.686	242.116
1001 to 2000	103.445	74.646	1.390	0.166	-42.862	249.751
2001 to 3000	115.571	76.064	1.520	0.129	-33.515	264.657
> 3000	262.307	72.008	3.640	<0.001	121.173	403.442
Dependent of Active Duty	Referent Group					
Retired	165.613	130.624	1.270	0.205	-90.410	421.635
Dependent of Retired	43.219	33.934	1.270	0.203	-23.291	109.729
Active Duty	-12.111	38.150	-0.320	0.751	-86.885	62.662
5 to 12 years						
13 to 18 years	-91.559	33.498	-2.730	0.006	-157.215	-25.904
19 to 40 years	13.163	30.312	0.430	0.664	-46.249	72.575
Lead agent	165.137	34.635	4.770	<0.001	97.253	233.021
Severity index	6.902	23.998	0.290	0.774	-40.134	53.938
constant	222.507	82.165	2.710	0.007	61.465	383.549

Table F-S2: OLS regression model predicting number of encounters adjusting for severity (more than three visits in before period)

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.083	0.048	1.710	0.088	-0.012	0.177
Encounters - before	0.544	0.004	152.750	<0.001	0.537	0.551
Males	0.151	0.050	3.010	0.003	0.053	0.250
Comorbidity	-0.309	0.045	-6.840	<0.001	-0.397	-0.220
Region 1	Referent Group					
Region 2	0.265	0.093	2.870	0.004	0.084	0.447
Region 3	-0.174	0.097	-1.790	0.073	-0.364	0.016
Region 4	-0.061	0.122	-0.500	0.616	-0.299	0.177
Region 5	0.004	0.117	0.030	0.975	-0.226	0.234
Region 6	-0.083	0.091	-0.920	0.357	-0.261	0.094
Region 7/8	0.085	0.090	0.940	0.345	-0.091	0.260
Region 9	-0.062	0.105	-0.590	0.558	-0.268	0.145
Region 10	0.046	0.169	0.270	0.788	-0.286	0.378
Region 11	-0.392	0.128	-3.070	0.002	-0.643	-0.142
Non-conus	0.243	0.088	2.760	0.006	0.071	0.416
Multiple facilities	0.706	0.057	12.300	<0.001	0.594	0.819
0 to 250	Referent Group					
251 to 500	0.282	0.183	1.540	0.123	-0.076	0.640
501 to 1000	0.489	0.168	2.910	0.004	0.159	0.818
1001 to 2000	0.626	0.150	4.180	<0.001	0.333	0.920
2001 to 3000	0.651	0.153	4.260	<0.001	0.352	0.951
> 3000	0.756	0.145	5.230	<0.001	0.473	1.040
Dependent of Active Duty	Referent Group					
Retired	0.213	0.262	0.810	0.416	-0.301	0.728
Dependent of Retired	0.104	0.068	1.520	0.128	-0.030	0.237
Active Duty	-0.389	0.077	-5.070	<0.001	-0.539	-0.239
5 to 12 years	Referent Group					
13 to 18 years	-0.830	0.067	-12.340	<0.001	-0.962	-0.698
19 to 40 years	0.025	0.061	0.420	0.678	-0.094	0.145
Lead agent	0.016	0.070	0.240	0.813	-0.120	0.153
Severity index	-1.815	0.057	-31.810	<0.001	-1.927	-1.703
Constant	2.679	0.166	16.150	<0.001	2.354	3.004

Table F-S3: OLS regression model predicting total visits adjusting for severity (more than three visits in the before period)

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.118	0.023	5.040	<0.001	0.072	0.164
Visits - before	0.274	0.004	64.190	<0.001	0.266	0.283
Males	-0.056	0.024	-2.300	0.021	-0.104	-0.008
Comorbidity	0.406	0.022	18.780	<0.001	0.363	0.448
Region 1	Referent Group					
Region 2	0.202	0.045	4.500	<0.001	0.114	0.289
Region 3	-0.212	0.047	-4.500	<0.001	-0.304	-0.120
Region 4	0.098	0.059	1.660	0.097	-0.018	0.213
Region 5	0.051	0.057	0.890	0.373	-0.061	0.162
Region 6	-0.072	0.044	-1.630	0.103	-0.158	0.014
Region 7/8	-0.106	0.043	-2.440	0.015	-0.191	-0.021
Region 9	0.210	0.051	4.110	<0.001	0.110	0.310
Region 10	0.056	0.082	0.680	0.497	-0.105	0.216
Region 11	-0.231	0.062	-3.730	<0.001	-0.352	-0.110
Non-conus	0.247	0.043	5.800	<0.001	0.164	0.331
Multiple facilities	0.532	0.028	19.110	<0.001	0.477	0.587
0 to 250	Referent Group					
251 to 500	0.155	0.089	1.750	0.081	-0.019	0.328
501 to 1000	0.306	0.081	3.760	<0.001	0.146	0.465
1001 to 2000	0.389	0.073	5.360	<0.001	0.247	0.531
2001 to 3000	0.541	0.074	7.310	<0.001	0.396	0.686
> 3000	0.711	0.070	10.150	<0.001	0.574	0.848
Dependent of Active Duty	Referent Group					
Retired	-0.192	0.127	-1.510	0.132	-0.441	0.057
Dependent of Retired	-0.009	0.033	-0.260	0.795	-0.073	0.056
Active Duty	0.048	0.037	1.280	0.199	-0.025	0.120
5 to 12 years	Referent Group					
13 to 18 years	-0.381	0.033	-11.690	<0.001	-0.445	-0.317
19 to 40 years	-0.198	0.029	-6.710	<0.001	-0.256	-0.140
Lead agent	-0.003	0.034	-0.090	0.929	-0.069	0.063
Severity index	-0.537	0.029	-18.220	<0.001	-0.595	-0.479
constant	0.589	0.080	7.370	<0.001	0.432	0.746

Table F-S4: OLS regression model predicting total prescriptions adjusting for severity (more than three visits in the before period)

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.008	0.036	0.230	0.821	-0.062	0.078
Visits - before	0.616	0.003	196.700	<0.001	0.610	0.622
Males	0.162	0.037	4.390	<0.001	0.090	0.235
Comorbidity	-0.514	0.033	-15.370	<0.001	-0.580	-0.449
Region 1	Referent group					
Region 2	0.082	0.068	1.210	0.226	-0.051	0.216
Region 3	0.055	0.071	0.770	0.440	-0.085	0.195
Region 4	-0.044	0.089	-0.490	0.624	-0.219	0.131
Region 5	-0.089	0.086	-1.030	0.301	-0.258	0.080
Region 6	0.029	0.067	0.430	0.667	-0.102	0.159
Region 7/8	0.218	0.066	3.310	0.001	0.089	0.347
Region 9	-0.249	0.077	-3.210	0.001	-0.400	-0.097
Region 10	0.051	0.125	0.410	0.682	-0.193	0.295
Region 11	-0.179	0.094	-1.910	0.056	-0.363	0.005
Non-conus	0.011	0.065	0.180	0.860	-0.115	0.138
Multiple facilities	0.217	0.042	5.150	<0.001	0.135	0.300
0 to 250	Referent group					
251 to 500	0.141	0.134	1.050	0.295	-0.123	0.404
501 to 1000	0.196	0.123	1.580	0.113	-0.046	0.438
1001 to 2000	0.255	0.110	2.310	0.021	0.039	0.471
2001 to 3000	0.131	0.112	1.170	0.242	-0.089	0.352
> 3000	0.131	0.106	1.230	0.217	-0.077	0.340
Dependent of Active Duty	Referent group					
Retired	0.392	0.193	2.030	0.042	0.014	0.770
Dependent of Retired	0.074	0.050	1.480	0.138	-0.024	0.173
Active Duty	-0.348	0.056	-6.160	<0.001	-0.458	-0.237
5 to 12 years	Referent group					
13 to 18 years	-0.452	0.049	-9.140	<0.001	-0.549	-0.355
19 to 40 years	0.199	0.045	4.440	<0.001	0.111	0.287
Lead agent	0.006	0.051	0.120	0.901	-0.094	0.107
Severity index	-0.451	0.038	-11.930	<0.001	-0.525	-0.377
constant	1.933	0.122	15.840	<0.001	1.694	2.173

Table F-E1: OLS regression model predicting total cost adjusting for severity using number of exacerbations in the before period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-59.47716	24.034	-2.470	0.013	-106.584	-12.370
Cost - before	0.2419937	0.003	70.060	0.000	0.235	0.249
Males	-23.54095	24.988	-0.940	0.346	-72.517	25.435
Comorbidity	6.173437	22.153	0.280	0.781	-37.247	49.594
Region 1	Referent group					
Region 2	-82.88614	46.000	-1.800	0.072	-173.046	7.273
Region 3	-147.605	48.288	-3.060	0.002	-242.249	-52.961
Region 4	-111.1868	60.426	-1.840	0.066	-229.621	7.247
Region 5	-108.2619	58.332	-1.860	0.063	-222.592	6.069
Region 6	-125.4846	44.997	-2.790	0.005	-213.679	-37.291
Region 7/8	-96.17269	44.538	-2.160	0.031	-183.466	-8.879
Region 9	-123.2782	52.282	-2.360	0.018	-225.750	-20.806
Region 10	-169.6402	84.161	-2.020	0.044	-334.595	-4.686
Region 11	-256.5022	63.433	-4.040	<0.001	-380.830	-132.174
Non-conus	-24.37297	43.769	-0.560	0.578	-110.160	61.414
Multiple facilities	201.5392	28.347	7.110	<0.001	145.979	257.100
0 to 250	Referent group					
251 to 500	83.59653	90.830	0.920	0.357	-94.429	261.622
501 to 1000	75.32795	83.470	0.900	0.367	-88.273	238.929
1001 to 2000	94.51195	74.505	1.270	0.205	-51.518	240.542
2001 to 3000	113.1509	75.919	1.490	0.136	-35.651	261.953
> 3000	226.1802	71.886	3.150	0.002	85.284	367.076
Dependent of Active Duty	Referent group					
Retired	155.0416	130.394	1.190	0.234	-100.530	410.613
Dependent of Retired	36.80682	33.875	1.090	0.277	-29.589	103.203
Active Duty	0.5161082	38.081	0.010	0.989	-74.122	75.155
5 to 12 years	Referent group					
13 to 18 years	-93.52016	33.400	-2.800	0.005	-158.985	-28.056
19 to 40 years	6.671045	30.240	0.220	0.825	-52.600	65.942
Lead agent	158.6998	34.565	4.590	<0.001	90.953	226.447
Exacerbation in before period	444.4005	27.787	15.990	<0.001	389.939	498.862
Constant	242.9479	81.876	2.970	0.003	82.471	403.425

Table F-E2: OLS regression model predicting number of encounters adjusting for severity using number of exacerbations in the before period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.075	0.049	1.540	0.123	-0.020	0.171
Encounters-before	0.487	0.003	159.900	<0.001	0.481	0.493
Males	0.209	0.051	4.130	<0.001	0.110	0.308
Comorbidity	-0.498	0.045	-11.040	<0.001	-0.586	-0.409
Region 1	Referent Group					
Region 2	0.359	0.093	3.860	<0.001	0.177	0.542
Region 3	-0.166	0.098	-1.690	0.090	-0.357	0.026
Region 4	-0.070	0.122	-0.570	0.567	-0.310	0.170
Region 5	-0.001	0.118	-0.010	0.994	-0.232	0.231
Region 6	-0.116	0.091	-1.270	0.203	-0.295	0.063
Region 7/8	0.075	0.090	0.830	0.408	-0.102	0.251
Region 9	-0.017	0.106	-0.160	0.873	-0.225	0.191
Region 10	0.011	0.170	0.070	0.947	-0.323	0.345
Region 11	-0.373	0.128	-2.910	0.004	-0.625	-0.122
Non-conus	0.258	0.089	2.910	0.004	0.085	0.432
Multiple facilities	0.551	0.058	9.560	<0.001	0.438	0.664
0 to 250	Referent Group					
251 to 500	0.278	0.184	1.510	0.131	-0.083	0.638
501 to 1000	0.432	0.169	2.560	0.011	0.101	0.764
1001 to 2000	0.563	0.151	3.730	<0.001	0.267	0.858
2001 to 3000	0.594	0.154	3.860	<0.001	0.292	0.895
> 3000	0.700	0.146	4.810	<0.001	0.415	0.985
Dependent of Active Duty	Referent Group					
Retired	0.336	0.264	1.270	0.204	-0.182	0.853
Dependent of Retired	0.152	0.069	2.220	0.026	0.018	0.287
Active Duty	-0.498	0.077	-6.460	<0.001	-0.650	-0.347
5 to 12 years	Referent Group					
13 to 18 years	-0.739	0.068	-10.920	<0.001	-0.872	-0.606
19 to 40 years	0.129	0.061	2.110	0.035	0.009	0.249
Lead agent	0.039	0.070	0.550	0.581	-0.099	0.176
Exacerbation in before period	-0.454	0.047	-9.560	<0.001	-0.547	-0.361
constant	2.659	0.167	15.920	<0.001	2.332	2.987

Table F-E3: OLS regression model predicting number of visits adjusting for severity using number of exacerbations in the before period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.122	0.023	5.220	<0.001	0.076	0.169
Visits - before	0.230	0.003	66.110	<0.001	0.223	0.237
Males	-0.050	0.024	-2.060	0.039	-0.098	-0.002
Comorbidity	0.394	0.022	18.160	<0.001	0.351	0.436
Region 1	Referent group					
Region 2	0.225	0.045	5.000	<0.001	0.137	0.313
Region 3	-0.207	0.047	-4.380	<0.001	-0.299	-0.114
Region 4	0.111	0.059	1.870	0.061	-0.005	0.226
Region 5	0.047	0.057	0.820	0.411	-0.065	0.159
Region 6	-0.077	0.044	-1.750	0.080	-0.163	0.009
Region 7/8	-0.106	0.044	-2.430	0.015	-0.191	-0.021
Region 9	0.229	0.051	4.480	<0.001	0.129	0.329
Region 10	0.058	0.082	0.710	0.478	-0.103	0.219
Region 11	-0.224	0.062	-3.610	<0.001	-0.345	-0.102
Non-conus	0.251	0.043	5.870	<0.001	0.167	0.335
Multiple facilities	0.494	0.028	17.740	<0.001	0.439	0.548
0 to 250	Referent group					
251 to 500	0.156	0.089	1.750	0.080	-0.018	0.329
501 to 1000	0.293	0.082	3.590	<0.001	0.133	0.453
1001 to 2000	0.374	0.073	5.140	<0.001	0.232	0.517
2001 to 3000	0.528	0.074	7.120	<0.001	0.382	0.673
> 3000	0.704	0.070	10.020	<0.001	0.566	0.841
Dep of Active Duty	Referent group					
Retired	-0.173	0.127	-1.360	0.174	-0.423	0.076
Dep of Retired	-0.004	0.033	-0.120	0.901	-0.069	0.061
Active Duty	0.036	0.037	0.960	0.335	-0.037	0.109
5 to 12 years	Referent group					
13 to 18 years	-0.358	0.033	-10.960	<0.001	-0.422	-0.294
19 to 40 years	-0.177	0.030	-6.010	<0.001	-0.235	-0.120
Lead agent	-0.006	0.034	-0.160	0.869	-0.072	0.061
Exacerbation in before period	-0.103	0.023	-4.430	<0.001	-0.149	-0.058
constant	0.537	0.080	6.700	<0.001	0.380	0.694

Table F-E4: OLS regression model predicting number of prescriptions dispensed adjusting for severity using number of exacerbations in the before period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0043	0.0356	0.120	0.903	-0.0654	0.0741
Prescriptions - before	0.6022	0.0029	206.300	<0.001	0.5964	0.6079
Males	0.1769	0.0370	4.780	<0.001	0.1043	0.2495
Comorbidity	-0.5623	0.0333	-16.900	<0.001	-0.6275	-0.4970
Region 1	Referent group					
Region 2	0.0999	0.0681	1.470	0.142	-0.0336	0.2334
Region 3	0.0537	0.0715	0.750	0.453	-0.0865	0.1938
Region 4	-0.0523	0.0895	-0.580	0.559	-0.2277	0.1231
Region 5	-0.0881	0.0864	-1.020	0.308	-0.2574	0.0812
Region 6	0.0123	0.0666	0.180	0.854	-0.1183	0.1429
Region 7/8	0.2113	0.0659	3.200	0.001	0.0821	0.3406
Region 9	-0.2326	0.0775	-3.000	0.003	-0.3845	-0.0808
Region 10	0.0441	0.1246	0.350	0.724	-0.2002	0.2883
Region 11	-0.1721	0.0939	-1.830	0.067	-0.3563	0.0120
Non-conus	0.0072	0.0648	0.110	0.911	-0.1198	0.1342
Multiple facilities	0.1640	0.0420	3.900	<0.001	0.0816	0.2464
0 to 250	Referent group					
251 to 500	0.1407	0.1345	1.050	0.296	-0.1229	0.4043
501 to 1000	0.1780	0.1236	1.440	0.150	-0.0642	0.4203
1001 to 2000	0.2326	0.1103	2.110	0.035	0.0163	0.4488
2001 to 3000	0.1108	0.1124	0.990	0.324	-0.1096	0.3311
> 3000	0.0973	0.1064	0.910	0.361	-0.1113	0.3059
Dependent of Active Duty	Referent group					
Retired	0.4128	0.1931	2.140	0.033	0.0343	0.7913
Dependent of Retired	0.0854	0.0502	1.700	0.089	-0.0129	0.1838
Active Duty	-0.3742	0.0564	-6.630	<0.001	-0.4848	-0.2636
5 to 12 years	Referent group					
13 to 18 years	-0.4253	0.0495	-8.600	<0.001	-0.5222	-0.3283
19 to 40 years	0.2238	0.0448	5.000	<0.001	0.1360	0.3116
Lead agent	0.0018	0.0512	0.040	0.972	-0.0986	0.1023
Exacerbation in before period	-0.0231	0.0343	-0.670	0.501	-0.0903	0.0441
constant	1.9079	0.1222	15.620	<0.001	1.6685	2.1473

Table F-B1: OLS regression model predicting cost of asthma therapy adjusting for severity using the number of β -agonist prescriptions dispensed in the before period

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-56.735	24.067	-2.360	0.018	-103.907	-9.563
Cost - before	0.270	0.003	93.640	<0.001	0.265	0.276
Males	-28.561	25.052	-1.140	0.254	-77.663	20.541
Comorbidity	25.315	22.608	1.120	0.263	-18.995	69.626
Region 1	Referent Group					
Region 2	-62.320	46.045	-1.350	0.176	-152.567	27.928
Region 3	-128.773	48.340	-2.660	0.008	-223.520	-34.026
Region 4	-108.021	60.511	-1.790	0.074	-226.623	10.580
Region 5	-90.526	58.407	-1.550	0.121	-205.003	23.951
Region 6	-117.827	45.059	-2.610	0.009	-206.144	-29.511
Region 7/8	-90.186	44.599	-2.020	0.043	-177.599	-2.773
Region 9	-111.992	52.353	-2.140	0.032	-214.603	-9.382
Region 10	-165.679	84.282	-1.970	0.049	-330.870	-0.487
Region 11	-228.810	63.509	-3.600	<0.001	-353.287	-104.332
Non-conus	-4.349	43.809	-0.100	0.921	-90.214	81.517
Multiple facilities	197.546	28.414	6.950	<0.001	141.854	253.239
0 to 250	Referent Group					
251 to 500	79.557	90.958	0.870	0.382	-98.720	257.834
501 to 1000	79.462	83.588	0.950	0.342	-84.370	243.294
1001 to 2000	103.497	74.608	1.390	0.165	-42.735	249.729
2001 to 3000	116.164	76.027	1.530	0.127	-32.848	265.176
> 3000	263.446	71.951	3.660	<0.001	122.422	404.469
Dep of Active Duty	Referent Group					
Retired	145.065	130.608	1.110	0.267	-110.926	401.055
Dep of Retired	33.122	33.949	0.980	0.329	-33.419	99.663
Active Duty	1.998	38.175	0.050	0.958	-72.825	76.821
5 to 12 years	Referent Group					
13 to 18 years	-101.421	33.473	-3.030	0.002	-167.027	-35.815
19 to 40 years	1.311	30.322	0.040	0.966	-58.121	60.743
Lead agent	159.753	34.620	4.610	<0.001	91.898	227.608
Bronchodilators in before period	29.144	4.032	7.230	<0.001	21.241	37.046
constant	158.498	82.482	1.920	0.055	-3.166	320.162

APPENDIX G:
OLS REGRESSION MODEL PREDICTING COST ADJUSTING
FOR THE ADDITIONAL COVARIATES OF TOTAL
VISITS AND PRESCRIPTIONS IN THE BEFORE PERIOD.

Table G1: OLS untransformed model predicting total costs in after period. Adjusting for the additional covariates of 'total visits' and 'prescriptions dispensed' in the before period.

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-54.402	24.069	-2.260	0.024	-101.578	-7.226
Cost - before	0.263	0.003	85.120	<0.001	0.257	0.269
Males	-26.457	25.045	-1.060	0.291	-75.545	22.630
Comorbidity	12.189	22.693	0.540	0.591	-32.289	56.666
Region 1	Referent group					
Region 2	-65.078	46.028	-1.410	0.157	-155.292	25.136
Region 3	-125.115	48.322	-2.590	0.010	-219.826	-30.404
Region 4	-106.640	60.511	-1.760	0.078	-225.242	11.962
Region 5	-82.105	58.390	-1.410	0.160	-196.550	32.340
Region 6	-123.789	45.053	-2.750	0.006	-212.093	-35.485
Region 7/8	-93.884	44.585	-2.110	0.035	-181.270	-6.498
Region 9	-91.094	52.374	-1.740	0.082	-193.747	11.560
Region 10	-163.284	84.258	-1.940	0.053	-328.429	1.861
Region 11	-214.130	63.505	-3.370	0.001	-338.599	-89.661
Non-conus	-7.077	43.792	-0.160	0.872	-92.910	78.755
Multiple facilities	179.028	28.521	6.280	<0.001	123.127	234.929
0 to 250	Referent group					
251 to 500	78.113	90.919	0.860	0.390	-100.089	256.314
501 to 1000	75.597	83.554	0.900	0.366	-88.170	239.363
1001 to 2000	96.678	74.582	1.300	0.195	-49.503	242.860
2001 to 3000	107.227	76.001	1.410	0.158	-41.735	256.188
> 3000	244.917	71.956	3.400	0.001	103.883	385.951
Dependent of Active Duty	Referent group					
Retired	134.396	130.563	1.030	0.303	-121.506	390.298
Dependent of Retired	35.829	33.927	1.060	0.291	-30.667	102.325
Active Duty	-6.632	38.176	-0.170	0.862	-81.456	68.192
5 to 12 years	Referent group					
13 to 18 years	-82.304	33.450	-2.460	0.014	-147.865	-16.742
19 to 40 years	12.584	30.290	0.420	0.678	-46.783	71.952
Lead agent	147.081	34.649	4.240	<0.001	79.169	214.992
Visits in before period	21.575	3.961	5.450	<0.001	13.811	29.340
Prescriptions in before period	14.161	2.126	6.660	<0.001	9.994	18.328
constant	122.540	82.587	1.480	0.138	-39.330	284.411

APPENDIX H:
REGRESSION MODELS UTILIZING A MODIFIED FORM OF THE
COMORBIDITY VARIABLE.
(CHRONIC SINUSITIS, BRONCHITIS, AND COPD)

Table H-1: OLS untransformed model predicting total costs in after period. Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-55.6104	24.061	-2.310	0.021	-102.770	-8.451
Cost - before	0.2728	0.003	94.990	<0.001	0.267	0.278
Males	-18.2016	25.005	-0.730	0.467	-67.211	30.808
Chronic Comorbidity	209.3027	70.884	2.950	0.003	70.370	348.235
Region 1	Referent					
Region 2	-61.0094	46.052	-1.320	0.185	-151.270	29.252
Region 3	-129.5501	48.359	-2.680	0.007	-224.333	-34.767
Region 4	-105.2791	60.527	-1.740	0.082	-223.911	13.353
Region 5	-93.4739	58.420	-1.600	0.110	-207.977	21.030
Region 6	-112.2370	45.066	-2.490	0.013	-200.567	-23.907
Region 7/8	-90.5047	44.617	-2.030	0.043	-177.953	-3.056
Region 9	-114.8984	52.369	-2.190	0.028	-217.542	-12.254
Region 10	-165.9800	84.314	-1.970	0.049	-331.236	-0.724
Region 11	-237.0005	63.534	-3.730	<0.001	-361.526	-112.475
Non-conus	-1.7284	43.812	-0.040	0.969	-87.600	84.143
Multiple facilities	205.4092	28.371	7.240	<0.001	149.803	261.016
0 to 250	Referent					
251 to 500	75.5914	90.987	0.830	0.406	-102.743	253.926
501 to 1000	75.3501	83.601	0.900	0.367	-88.509	239.209
1001 to 2000	102.6977	74.624	1.380	0.169	-43.564	248.960
2001 to 3000	112.4748	76.043	1.480	0.139	-36.570	261.519
> 3000	259.0034	71.972	3.600	<0.001	117.938	400.069
Dependent of Active Duty	Referent					
Retired	166.7173	130.590	1.280	0.202	-89.238	422.673
Dependent of Retired	43.8996	33.927	1.290	0.196	-22.597	110.396
Active Duty	-9.6501	38.141	-0.250	0.800	-84.406	65.106
5 to 12 years	Referent					
13 to 18 years	-92.8410	33.451	-2.780	0.006	-158.404	-27.278
19 to 40 years	6.8938	30.339	0.230	0.820	-52.571	66.359
Lead agent	163.2568	34.626	4.710	<0.001	95.390	231.124
constant	221.0429	81.045	2.730	0.006	62.194	379.891

Table H-2: OLS untransformed model predicting total encounters in after period. Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0893	0.049	1.830	0.067	-0.006	0.185
Encounters - before	0.4851	0.003	162.670	<0.001	0.479	0.491
Males	0.2334	0.051	4.610	<0.001	0.134	0.333
Chronic Comorbidity	0.1681	0.143	1.170	0.241	-0.113	0.449
Region 1	Referent					
Region 2	0.3515	0.093	3.770	<0.001	0.169	0.534
Region 3	-0.1879	0.098	-1.920	0.055	-0.380	0.004
Region 4	-0.0851	0.123	-0.690	0.487	-0.325	0.155
Region 5	-0.0283	0.118	-0.240	0.811	-0.260	0.204
Region 6	-0.1271	0.091	-1.390	0.164	-0.306	0.052
Region 7/8	0.0648	0.090	0.720	0.473	-0.112	0.242
Region 9	-0.0215	0.106	-0.200	0.839	-0.229	0.186
Region 10	0.0269	0.171	0.160	0.875	-0.308	0.361
Region 11	-0.4090	0.129	-3.180	0.001	-0.661	-0.157
Non-conus	0.2503	0.089	2.820	0.005	0.076	0.424
Multiple facilities	0.5138	0.058	8.920	<0.001	0.401	0.627
0 to 250	Referent					
251 to 500	0.2796	0.184	1.520	0.129	-0.081	0.641
501 to 1000	0.3895	0.169	2.300	0.021	0.058	0.721
1001 to 2000	0.5277	0.151	3.490	<0.001	0.232	0.824
2001 to 3000	0.5528	0.154	3.590	<0.001	0.251	0.855
> 3000	0.6248	0.146	4.290	<0.001	0.339	0.910
Dependent of Active Duty	Referent					
Retired	0.3798	0.264	1.440	0.151	-0.138	0.898
Dependent of Retired	0.1604	0.069	2.330	0.020	0.026	0.295
Active Duty	-0.4691	0.077	-6.070	<0.001	-0.620	-0.318
5 to 12 years	Referent					
13 to 18 years	-0.7250	0.068	-10.700	<0.001	-0.858	-0.592
19 to 40 years	0.0942	0.061	1.530	0.125	-0.026	0.215
Lead agent	0.0294	0.070	0.420	0.675	-0.108	0.167
constant	2.4086	0.165	14.600	<0.001	2.085	2.732

Table H-3: OLS untransformed model predicting total visits in after period.
Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.1071	0.024	4.560	<0.001	0.061	0.153
Visits - before	0.2288	0.003	68.020	<0.001	0.222	0.235
Males	-0.0696	0.024	-2.850	0.004	-0.118	-0.022
Chronic Comorbidity	0.4642	0.069	6.700	<0.001	0.328	0.600
Region 1	Referent					
Region 2	0.2042	0.045	4.540	<0.001	0.116	0.292
Region 3	-0.2135	0.047	-4.520	<0.001	-0.306	-0.121
Region 4	0.1161	0.059	1.960	0.050	0.000	0.232
Region 5	0.0545	0.057	0.950	0.340	-0.057	0.166
Region 6	-0.0816	0.044	-1.850	0.064	-0.168	0.005
Region 7/8	-0.1107	0.044	-2.540	0.011	-0.196	-0.025
Region 9	0.2194	0.051	4.280	<0.001	0.119	0.320
Region 10	0.0647	0.082	0.780	0.433	-0.097	0.226
Region 11	-0.2262	0.062	-3.640	<0.001	-0.348	-0.104
Non-conus	0.2285	0.043	5.340	<0.001	0.145	0.312
Multiple facilities	0.5108	0.028	18.330	<0.001	0.456	0.565
0 to 250	Referent					
251 to 500	0.1544	0.089	1.740	0.082	-0.020	0.329
501 to 1000	0.3153	0.082	3.860	<0.001	0.155	0.475
1001 to 2000	0.3889	0.073	5.330	<0.001	0.246	0.532
2001 to 3000	0.5443	0.074	7.320	<0.001	0.399	0.690
> 3000	0.7070	0.070	10.050	<0.001	0.569	0.845
Dep of Active Duty	Referent					
Retired	-0.2222	0.128	-1.740	0.082	-0.472	0.028
Dep of Retired	-0.0142	0.033	-0.430	0.669	-0.079	0.051
Active Duty	0.0355	0.037	0.950	0.341	-0.038	0.109
5 to 12 years	Referent					
13 to 18 years	-0.3740	0.033	-11.440	<0.001	-0.438	-0.310
19 to 40 years	-0.1782	0.030	-6.010	<0.001	-0.236	-0.120
Lead agent	-0.0253	0.034	-0.750	0.454	-0.092	0.041
constant	0.7677	0.079	9.670	<0.001	0.612	0.923

Table H-4: OLS untransformed model predicting total number of prescriptions in the after period. Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variables</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	0.0261	0.036	0.730	0.464	-0.044	0.096
Prescriptions - before	0.6104	0.003	212.720	<0.001	0.605	0.616
Males	0.2004	0.037	5.400	<0.001	0.128	0.273
Chronic Comorbidity	-0.0901	0.105	-0.860	0.391	-0.296	0.116
Region 1	Referent					
Region 2	0.1158	0.068	1.700	0.090	-0.018	0.249
Region 3	0.0530	0.072	0.740	0.459	-0.087	0.193
Region 4	-0.0582	0.090	-0.650	0.517	-0.234	0.118
Region 5	-0.1016	0.087	-1.170	0.240	-0.271	0.068
Region 6	0.0120	0.067	0.180	0.857	-0.119	0.143
Region 7/8	0.2095	0.066	3.170	0.002	0.080	0.339
Region 9	-0.2175	0.078	-2.800	0.005	-0.370	-0.065
Region 10	0.0542	0.125	0.430	0.664	-0.191	0.299
Region 11	-0.1784	0.094	-1.890	0.058	-0.363	0.006
Non-conus	0.0256	0.065	0.390	0.693	-0.102	0.153
Multiple facilities	0.1275	0.042	3.030	0.002	0.045	0.210
0 to 250	Referent					
251 to 500	0.1397	0.135	1.040	0.300	-0.124	0.404
501 to 1000	0.1390	0.124	1.120	0.262	-0.104	0.382
1001 to 2000	0.2054	0.111	1.860	0.063	-0.011	0.422
2001 to 3000	0.0752	0.113	0.670	0.504	-0.146	0.296
> 3000	0.0638	0.107	0.600	0.549	-0.145	0.273
Dependent of Active Duty	Referent					
Retired	0.4617	0.193	2.390	0.017	0.082	0.841
Dependent of Retired	0.0942	0.050	1.870	0.061	-0.004	0.193
Active Duty	-0.3550	0.057	-6.280	<0.001	-0.466	-0.244
5 to 12 years	Referent					
13 to 18 years	-0.4042	0.050	-8.160	<0.001	-0.501	-0.307
19 to 40 years	0.2024	0.045	4.500	<0.001	0.114	0.290
Lead agent	0.0067	0.051	0.130	0.895	-0.094	0.107
Constant	1.5578	0.121	12.920	<0.001	1.321	1.794

Table H-5: Logistic untransformed model predicting total exacerbations in after period. Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variable</i>	<i>Odds Ratio</i>	<i>Std. Error</i>	<i>z-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	1.201	0.070	3.150	0.002	1.071	1.346
Exacerbations - before	0.336	0.044	-8.310	<0.001	0.260	0.434
Males	1.048	0.065	0.750	0.452	0.928	1.183
Chronic Comorbidity	0.518	0.104	-3.280	0.001	0.349	0.767
Region 1	Referent					
Region 2	2.524	0.304	7.680	<0.001	1.993	3.197
Region 3	1.475	0.202	2.830	0.005	1.127	1.930
Region 4	1.426	0.232	2.180	0.029	1.037	1.962
Region 5	0.904	0.145	-0.630	0.531	0.660	1.239
Region 6	1.300	0.166	2.050	0.040	1.012	1.671
Region 7/8	1.451	0.182	2.960	0.003	1.134	1.856
Region 9	1.370	0.201	2.150	0.031	1.029	1.826
Region 10	0.229	0.091	-3.710	<0.001	0.105	0.499
Region 11	1.004	0.164	0.020	0.980	0.729	1.383
Non-conus	2.435	0.306	7.080	<0.001	1.903	3.116
Multiple facilities	0.977	0.068	-0.330	0.742	0.853	1.120
0 to 250	Referent					
251 to 500	0.194	0.217	-1.470	0.143	0.022	1.739
501 to 1000	2.472	1.370	1.630	0.102	0.834	7.326
1001 to 2000	5.213	2.662	3.230	0.001	1.916	14.182
2001 to 3000	3.574	1.855	2.450	0.014	1.293	9.882
> 3000	17.137	8.631	5.640	<0.001	6.386	45.985
Dependent of Active Duty	Referent					
Retired	0.702	0.211	-1.170	0.240	0.389	1.267
Dependent of Retired	1.276	0.097	3.220	0.001	1.100	1.480
Active Duty	0.782	0.071	-2.690	0.007	0.653	0.935
5 to 12 years	Referent					
13 to 18 years	0.969	0.081	-0.370	0.711	0.822	1.143
19 to 40 years	1.472	0.104	5.450	<0.001	1.281	1.692
Lead agent	1.713	0.112	8.260	<0.001	1.508	1.946

Table H-6: OLS untransformed model predicting total number of beddays in the after period. Comorbidity variable modified to include only subjects diagnosed with chronic sinusitis, bronchitis, or COPD.

<i>Variable</i>	<i>Coefficient</i>	<i>Std. Error</i>	<i>t-value</i>	<i>p-value</i>	<i>95% Confidence Interval</i>	
Cpg	-0.0060	0.004	-1.360	0.173	-0.015	0.003
Beddays - before	0.1094	0.002	46.210	<0.001	0.105	0.114
Males	-0.0136	0.005	-2.970	0.003	-0.023	-0.005
Chronic Comorbidity	0.0488	0.013	3.750	<0.001	0.023	0.074
Region 1	Referent					
Region 2	-0.0089	0.008	-1.050	0.295	-0.025	0.008
Region 3	-0.0051	0.009	-0.570	0.568	-0.022	0.012
Region 4	-0.0082	0.011	-0.730	0.463	-0.030	0.014
Region 5	-0.0197	0.011	-1.840	0.066	-0.041	0.001
Region 6	0.0002	0.008	0.030	0.977	-0.016	0.016
Region 7/8	-0.0069	0.008	-0.850	0.397	-0.023	0.009
Region 9	-0.0120	0.010	-1.250	0.211	-0.031	0.007
Region 10	-0.0248	0.015	-1.600	0.109	-0.055	0.006
Region 11	-0.0403	0.012	-3.450	0.001	-0.063	-0.017
Non-conus	0.0136	0.008	1.690	0.091	-0.002	0.029
Multiple facilities	0.0347	0.005	6.650	<0.001	0.024	0.045
0 to 250	Referent					
251 to 500	0.0022	0.017	0.130	0.894	-0.031	0.035
501 to 1000	0.0090	0.015	0.590	0.558	-0.021	0.039
1001 to 2000	0.0179	0.014	1.310	0.191	-0.009	0.045
2001 to 3000	0.0143	0.014	1.020	0.307	-0.013	0.042
> 3000	0.0477	0.013	3.600	<0.001	0.022	0.074
Dependent of Active Duty	Referent					
Retired	-0.0028	0.024	-0.120	0.907	-0.050	0.044
Dependent of Retired	0.0074	0.006	1.190	0.233	-0.005	0.020
Active Duty	-0.0071	0.007	-1.010	0.313	-0.021	0.007
5 to 12 years	Referent					
13 to 18 years	0.0097	0.006	1.570	0.115	-0.002	0.022
19 to 40 years	0.0283	0.006	5.080	<0.001	0.017	0.039
Lead agent	0.0652	0.006	10.250	<0.001	0.053	0.078
constant	-0.0207	0.015	-1.390	0.165	-0.050	0.008

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EFFECTIVENESS OF CLINICAL PRACTICE GUIDELINES FOR TREATING
ASTHMA IN THE DEPARTMENT OF DEFENSE: A COMPARISON OF CLINICAL
AND ECONOMIC OUTCOMES BETWEEN THE ARMY, AIR FORCE, AND NAVY

David McAlpine Bennett, Ph.D.

The University of Arizona, 2002

Director: Daniel C. Malone

The purpose of this research was to evaluate the strategy of the military health service (MHS) to improve asthma outcomes through the use of clinical practice guidelines (CPGs). Outcomes were evaluated at the patient level and included inpatient/outpatient visits, prescriptions dispensed, number of exacerbations, number of beddays and direct cost of therapy. In addition, provider compliance to CPG recommendations was evaluated by measuring the proportion of subjects dispensed long-acting controller medications. A nonrandomized control-group before-after design with retrospective matched-pair DoD data was used for this research. The intervention used in this research was the formal asthma CPG-use process implemented by the Army in September of 2000.

Compared to baseline measures, all outcomes improved significantly ($p < 0.05$) in the after period for both the subjects exposed, and not exposed, to the CPG-use process. Other than the improvement noted in the number of asthma exacerbations, which was

greater in the exposed group than the non-exposed group ($p < 0.001$), there was no other difference between groups in the amount that outcomes improved.

When adjusted for covariates (gender, comorbidity, age, beneficiary status, facility size, TRICARE region, multiple facilities, and treatment received at a lead agent facility), the CPG-use process was associated with a decrease in the direct cost of asthma therapy (-\$55.65, $p = 0.021$). There was no association between the Army CPG-use process and total number of encounters, prescriptions, or beddays. Health care visits (0.12, $p < 0.001$) and exacerbations (OR = 1.22, $p < 0.001$) were significantly higher for those exposed to the CPG-use process as compared to those not exposed.

The proportion of subjects prescribed long-term controller medications increased significantly for subjects exposed to the CPG-use process (0.30 to 0.66, $p < 0.001$), and for those not exposed to the CPG-use process (0.30 to 0.66, $p < 0.001$).

Although the findings of this research suggested that a formal CPG-use process to standardize asthma therapy was associated with decreased costs, this was not supported by results regarding the clinical outcomes. To further evaluate the effect of asthma CPGs on economic and clinical outcomes, additional research is needed.

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Thursday, July 18, 2002

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Graduate Degree Certification

CERTIFICATE OF COMPLETION OF DEGREE REQUIREMENTS

This is to certify that

David McAlpine Bennett, Jr.

Completed requirements on: **Thursday, July 18, 2002**

for the degree of: **Doctor of Philosophy**

Major: **Pharmaceutical Sciences**

Minor: **Epidemiology**

The degree will be conferred on: **Thursday, August 08, 2002**

This form is official only when embossed with The University of
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Student Academic Specialist



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